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ditor:—Lieut Colonel JASWANT SINGH M B Ch B D P H, D T M & H,
Director Malaria Institute of India, Delhi



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MANUSCRIPT

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Tables, charts, etc., should be numbered, and alluded to in the text as 'Table I', etc., and not as 'the following table', etc.

ABBREVIATIONS, ETC.

The following contractions are in use in the *Indian Journal of Malariology*, whether the number to be expressed is one or more :—

gramme, gm.; kilogramme, kg.; centigramme, cg.; milligramme, mg.; metre, m.; kilometre, km.; centimetre, cm.; millimetre, mm.; cubic centimetre, c.c.; cubic millimetre, c.mm.; cubic foot, c.ft.

N.B.—In order to avoid ambiguity the word 'grain' should be written in full.

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The title may be omitted, but the reference should always give author's name, year, abbreviated [illegible] y type [illegible] year [illegible] d case, [illegible]

The following are some of the abbreviations in use :—

Amer. J. Hyg.
Ann. Trop. Med. Parasit.
Brit. Med. J.
Bull. Ent. Res.
Bull. Soc. Path. Exot.
C. R. Soc. Biol.
Geneesk. Tijd. Ned.-Ind.
Ind. J. Mal.
Ind. J. Med. Res.
J. Mal. Inst. Ind.
Jl. R. A. M. C.
J. Trop. Med. Hyg.
Meded. Volk. Ned. Ind.
Rec. Mal. Surv. Ind.
Rev. App. Ent.
Riv. Malariol.
Trans. Roy. Soc. Trop. Med. Hyg.
Trop. Dis. Bull.
U.S.A. Pub. Hlth. Rpts.

Indian Journal of Malariology, 9, 4, December 1955

CONTENTS

NOTICE.

The *Indian Journal of Malariology* is published four times a year, in March, June, September and December Each volume consists of four numbers

Articles for publication and Journals sent in exchange should be addressed to the 'Director, Malaria Institute of India, Delhi', from whom all information regarding the Journal may be obtained Purely business communications and applications for copies of the Journal should be addressed to Messrs Job Press Limited, Kanpur, to whom also subscriptions should be paid

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PLATE III



B gad er J A SINTON V C O B E M S (Retd)
Ed tor 19 J 1935

EDITORIAL

THE *Indian Journal of Malariology* has successfully completed 25 years of its service to the malaria world Starting as *Records of the Malaria Survey of India*, its nomenclature was changed to *Journal of the Malaria Institute of India* in 1938 and finally switched over to *Indian Journal of Malariology* in 1947.

So far 22 volumes, each consisting of four issues, have appeared It is a quarterly publication but in 1932-1933 and during the war years (1941-1946), when there was paucity of material for publication, one volume was completed in two years For the same reason, two issues were combined into one, four times during the entire period The total number of printed pages run to 11,506, average 523 pages per volume During this period, 805 articles have appeared, average 37 per volume (Table I)

TABLE I.

Number of articles and pages published

Volume	Year	Number of *articles*	Number of *pages*
Records of the Malaria Survey of India			
1	1929-30	33	771
2	1931	23	664
3	1932-33	39	856
4	1934	29	426
5	1935	32	528
6	1936	33	676
7	1937	21	272
Journal of the Malaria Institute of India			
1	1938	39	480
2	1939	36	463
3	1940	44	609
4	1941-42	43	642
5	1943-44	37	477
6	1945-46	42	513
Indian Journal of Malariology			
1	1947	41	517
2	1948	39	327
3	1949	35	426
4	1950	41	526
5	1951	28	604
6	1952	41	540
7	1953	50	392
8	1954	50	395
9	1955	41	402
Total		805	11,506
Average per volume		37	523

Articles published are not only accounts of work done by the staff of the Malaria Institute of India (formerly Malaria Survey of India) and other Indian workers, but the journal has enjoyed the confidence of eminent research workers in foreign countries as well and includes as many as 58 contributions from them as per following details —

		746
India	9	
Africa	1	
Belgium	1	
Burma	12	
Ceylon	6	
Formosa	3	
France	1	
Holland	4	
Indonesia	1	
Ireland	2	
Italy	1	
Malaya	1	
Nepal	2	
Pakistan	1	
Palestine	1	
Switzerland	8	
U K	4	58
U S A		804
	58	

So far, 28 abstracts of articles of local importance (the original MSS having been kept in the library of the Malaria Institute of India for reference by workers who wish to consult them) and nine obituaries of eminent workers who left a wide gap among the malariologists of the world, have appeared in the journal Review of important books has only recently been started and so far only four reviews have appeared

The total number of authors who have contributed to the journal from time to time is 365 The largest number of pages contributed by a single author so far is 1,057 in 43 articles by Major General Sir Gordon Covell (Director, Malaria Institute of India from 1936 to 1947) and the largest number of contributions by a single author is 83 comprising 759 pages by Lt -Colonel Jaswant Singh (Director, Malaria Institute of India from 1947 to date)

The subjects covered include malaria in all its aspects (human, avian, simian and recently rodent—physiology of malaria parasite, pathology, chemotherapy, immunology, epidemiology and control), studies on mosquitoes, both Culex and Anopheles (distribution, vectorial capacity, relation to malaria, destruction by the use of insecticides, resistance to insecticides), blackwater fever, kala azar, filariasis, etc

The Director, Malaria Institute of India, has been the ex officio editor of the journal Brigadier J A Sinton remained the editor from 1929 to 1935 and

PLATE IX



Ma r C n al S CORLON COVELL [illegible] R I
[illegible] 1936 1946

was assisted at times by Lt.-Colonel H. W. Mulligan during 1935. Major General Sir Gordon Covell took up the editorship in 1936 and continued till 1946. He was assisted by Lt.-Colonel M. K. Afridi up to 1939 and by Lt.-Colonel Jaswant Singh from 1941 onwards. Lt.-Colonel Jaswant Singh became the editor in 1947 and is still continuing.

The journal is financed by the Indian Council of Medical Research and besides money realized from sales, advertisements, etc., receives an annual grant of Rs. 12,500 per year for its publication only.

It has a world wide circulation and has a special place among the malaria publications. There are at present 70 foreign and 98 Indian subscribers. Besides 114 copies issued in exchange, 112 copies are distributed free to eminent workers and institutions both in India and abroad. A large number of journals of international repute are received in exchange of this journal, which considerably augment the resources of the library at the Malaria Institute of India.

With the formation of Malaria Survey of India in 1927, it was felt necessary to dig out the old reports and articles relating to malaria all over the country. Some of these were included in provincial publications and many were still in the MS. form. In the course of a three month tour throughout India, Sinton [illegible] *India* in 1929. In the second number, many [illegible] hich had appeared during previous years but were no longer available for general use, were reprinted.

There have been outstanding contributions by workers in India, *viz.*, malaria in Sind by *Sinton, Covell, and Baily*, *treatment with cinchona alkaloids* and what mal[illegible] contributions [illegible] Barraud, Cov[illegible] Iyengar, Muirhead-Thomson, Pal and others, monkey malaria and extensive [illegible] Vats, Jaswant Singh, [illegible] Wats, Paul Russell, [illegible] and others, malaria and its engineering aspects by Jaswant Singh, Henderson and others, studies on *Plasmodium berghei* by Ramakrishnan, Satya Prakash, Krishnaswami and colleagues, progress of antimalaria operations in Delhi by Covell, Afridi and Jaswant Singh, in Bombay by Viswanathan, Ramachandra Rao and colleagues, in Mysore by Sweet, Rao and others, on B. N. Railway by Senior White and co-workers. The study of malaria and its vectors in Borneo by McArthur and Colless, studies on the bionomics of *A. aquasalis* and its relation to malaria in British West Indies by Senior White, malaria in Formosa by Watson and colleagues, are some of the other notable contributions. Besides, special issues have been published from time to time on Paludrine, Insecticides, Pyrimethamine, Malaria in Ceylon, and a written symposium on *Plasmodium berghei* in which workers from all over the world participated.

The journal has been one of the most important organs of the East (perhaps the only one of its kind) for making known the trend of malaria research and control It has tried to help in the fulfilment of two of the main functions of the Malaria Institute of India (1) " To publish scientific results, useful guides, bulletins, etc ", and (2) " To keep alive interest in malaria study and prevention and to see that such interest, wherever present, is nursed and assisted ". If India has launched upon the most gigantic programme of malaria control, it is because the Malaria Institute of India has maintained a continuous propagation of ideas on malaria prevalence and its effects on the economy of the country, and in this the *Indian Journal of Malariology* has played a very prominent part It has kept up its standard through many hazards it had to face during the war years

The Jubilee Issue gives useful important reviews of the past researches and studies by eminent workers, and suggestions for the future on different aspects of the subject It also depicts the present position of malaria control and research and paves a way for future programmes It is a useful guide and a source of inspiration for those entering the field

Recently the activities of the Malaria Institute have expanded to include some of the other communicable diseases, and the Malaria Advisory Committee of the Indian Council of Medical Research has also been redesignated as " Malaria and other Arthropod-borne Diseases Sub Committee " of the Communicable Diseases Advisory Committee Whether the *Indian Journal of Malariology* should also widen its scope and welcome in its fold valuable knowledge about other arthropod-borne diseases and thus change its name once again, is a problem which will have to be considered in the near future

This period of 25 years has been of great interest not only for contributors and readers but also for those connected with editing of this publication Its future will no doubt be watched with interest

The editor solicits the cooperation and patronage of contributors, institutions engaged in research and control of arthropod-borne diseases and also of those who are interested in emancipating the world of the misery caused by many preventible diseases

Plate V



[illegible]

[illegible]

[illegible]

DO ALL THE HUMAN MALARIA PARASITES BELONG TO ONE GENUS?

As discussed by Christophers and Sinton (1938), Grassi and Feletti in 1890 divided the malaria parasites into two genera—first, *Hæmamœba* to include the

mere differences in the form of the gametocytes was sufficient to justify the erection of two separate genera He grouped all these parasites in the genus *Plasmodium* Marchiafava This ruling has been followed by most workers from that time

Since the discovery of the exo erythrocytic cycle of schizogony in malaria parasites, this problem needs reconsideration The latest classification of this type of schizogony, as given by the World Health Organization's Drafting Committee on "Malaria Terminology" (Covell, Russell and Swellengrebel, 1953), shows that of the human species of *Plasmodium* s s as quite different from that of *Laverania*

Now that the exoerythrocytic cycles of schizogony has been found to differ greatly in these two groups, does not this suggest that the classification given by Grassi and Feletti is justified? Should the genus *Laverania* be officially recognized as the correct name for such parasites as *Plasmodium falciparum* [vel *L malariæ* (Laveran)]

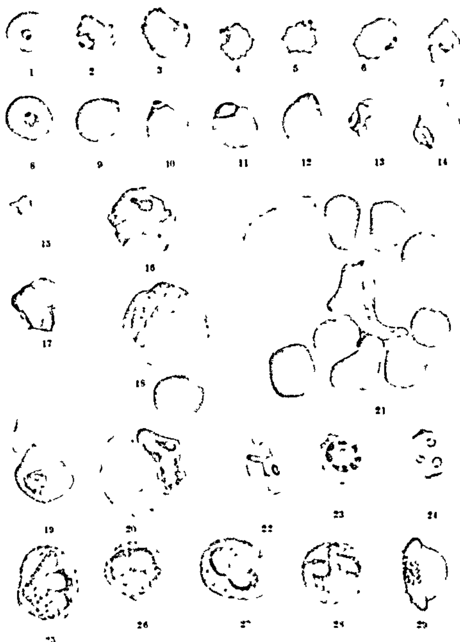
IS THE MALARIA PARASITE INSIDE OR OUTSIDE THE ERYTHROCYTE?

Laveran in his original description of the malaria parasites believed these to be extraglobular Most of the other older writers like Marchiafava and Bignami (1894) asserted that they were within the red blood cells Mannaberg (1894), however, thought that the *young* rings of the æstivo autumnal parasites were outside the erythrocyte

Maurer (1902), in his paper on the stippling of red cells infected with plasmodia, came to the conclusion that the large and small ring forms of the pernicious parasite remained extracellular while they were in the peripheral blood At the stage of development, however, when they disappeared into the internal organs, they entered the red cells

The description given by Schaudinn (1902) of the entry of the sporozoite and the merozoite into the erythrocyte seemed to settle their intracellular position definitely Rowley-Lawson (1914, 1918) again raised the question and produced evidence which cast doubt on the above finding

The question was re opened by Sinton (1922) He pointed out that, on account of the very thin flattened shape of the erythrocyte, it was impossible by microscopical examination to ascertain whether the parasite lay in or on the cell (Plate VI, Fig 1 and 8) He subjected the infested cells to hypertonic and hypotonic conditions to change their shape from a flat to a globular form In *falciparum* infections this caused a great increase in the number of accolé forms



Figs. 1 and 8 [illegible] forms of *P. falciparum*
Figs. 2-7 [illegible]
Figs. 9-13 [illegible]
Figs. 16-17 [illegible]
Figs. 18-20 [illegible]
Fig. 21 [illegible]
Fig. 22 [illegible]
Fig. 23 [illegible]
Fig. 24 Erythrocyte infected with [illegible]

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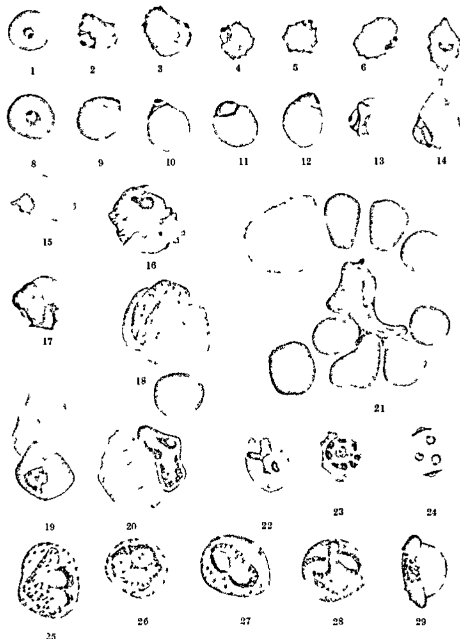
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FIGS 1 and 8

FIGS 2 7

FIGS 9-15

FIGS 16-17

FIGS 18 20

FIG 21

FIG 22 *P tenue* wit Maurer s dots in parasit zed erythrocyte

FIG 23 Mature schizont of *P tenue*

FIG 24 Erythrocyte infested with multiple rings of *P fal iparum*

FIGS 25 28 Early stages of division of *P tenuis* schizont

FIG 29 Gametocyte of *P falciparum* with red cell " bib "

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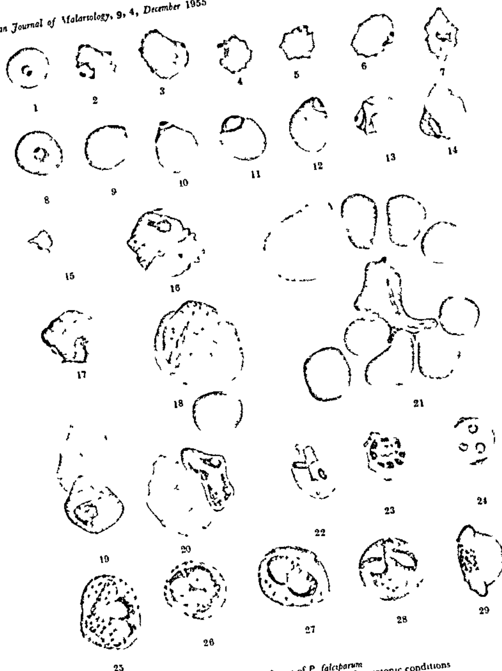
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Indian Journal of Malariology, 9, 4, December 1955



FIGS 1 and 8
FIGS 2 7
FIGS 9 15
FIGS 16-1‾
FIGS 18 20
FIG 21
FIG 2?
FIG 23
FIG 24
F 2 ?28

Erythrocytes with ring forms of *P falciparum*
Accole forms of *P falciparum* produced by hypertonic conditions
Accolé forms produced by hypotonic conditions
Extracellular forms of *P vivax* produced by hypotonic conditions
Extracellular forms of *P vivax* from moist chamber preparations
Extracellular forms of *P vivax* from its host cell under moist chamber conditions
P vivax migrating from its host cell under moist chamber conditions
P tenue with Maurer s dots in parasitized erythrocyte
Mature schizont of *P tenue*
Erythrocyte infested with multiple rings of *P falciparum*
Early stages of d vision of *P* ... sch
G metocyte of *P falciparum* with red ...

(Plate VI, Fig 2-7, 9-15) While in *vivax* infections hypotonic conditions caused many of the parasites to appear as if attached to the outside of the cell (Plate VI, Fig 16 and 17) He concluded that "results have been obtained which I am unable to explain satisfactorily except on the hypothesis that the sub-tertian and the benign tertian malarial parasites are, for the most of their asexual cycle in the human host, attached to the outer surfaces of the red blood cells" "These results are published in the hope that renewed interest will be stimulated in this problem and that further investigations will be made which will settle definitely the disputed point of the relative positions of the malarial parasite and the red blood corpuscle"

In his experiments, Sinton (1922) noted the extracellular position assumed by many of the parasites in thin films from *vivax* malaria when kept in a moist chamber Not on[illegible] e extracellular (Plate [illegible] he apparently unbrok[illegible] phenomenon must [illegible] flagellation of *P vivax* in a moist chamber *

Thomson and Woodcock (1922) thought that the majority of *vivax* parasites were intracellular, but that some completed their cycle extracellularly The parasites depicted by them in their Plate LXIV, Figs 38-42, are very similar to those produced by hypotonic conditions It is possible that slow drying in a moist atmosphere before fixation may have been the cause of these appearances

Schuffner and de Graaf (1937) also noted that quartan parasites freed themselves from their host cells in moist preparations

Sections of infected blood were made by Sinton (1922) and these appeared to support the extracellular theory Ratcliffe (1927 1928), however, did a much larger series of sectional experiments and concluded that the parasites were intracellular A critical study of the latter work shows that his sections were 2µ thick As the thickness of the erythrocyte is about 2 5µ at the periphery† and only 1 5µ at the centre red cells lying on the flat in sections would give the same appearance as these cells in thin films i e, intracellular It must also be remembered that blood cells placed in a fluid fixative usually become distorted—globular, cupshaped or irregular So in sections any parasites lying in such cupped cells would appear to be intracellular ‡

In the ca[illegible] the outline of t[illegible] if the cell was [illegible] position of the [illegible]

*Shute and Maryon (193[illegible]) while this paper was being prepared have called attention to these free parasites in moist films and consider that this suggests that the parasite is on and not in the red cell"

†In the abstract of Sinton's paper in the Tropical Diseases Bulletin the reviewer makes great play of the fact that the measurement µ was printed as mu The author was not responsible for this printer's error, which was not in the original manuscript

‡Since the above was written Fulton and Flewitt (195[illegible]) have used the electron microscope on sections 0 03-0 05 µ thick of red cells parasitized with *P berghei* and *P knowlesi* They conclude that all the evidence so far obtained by the methods employed indicates that the two parasites studied lie within the red cell"

Erythrocytes carrying multiple infections, even as many as six, are not rare in severe malignant tertian infections (Plate VI,, Fig 24) On the other hand, it is very rare to find even double infections with mature parasites of this species apart from any question of triple or quadruple ones What happens to the other parasites? Are they swept off the outside of the host cell and perish, or do they then acquire fresh host cells as suggested by Rowley Lawson (1914,1918)? It may be, of course, that so heavily burdened erythrocytes never emerge again into the peripheral blood from the internal organs, so escaping detection

While the extracellular position of the parasites may help to explain some problems, yet it is difficult to understand the position of mature parasites in double infections such as were mistaken by Schaudinn (1902) for parthenogenesis, except on the assumption that the parasites are held in position by a globular wall (*vide* Plate LXIV, Figs 44-47 of Thomson and Woodcock, 1922) Tobb

P ovale (Sinton, 1955)

Even as late as 1953, the Drafting Committee on " Malarial Terminology " appointed by the World Health Organization (Covell, Russell and Swellengrebel, 1953) are not agreed in an authoritative pronouncement on the matter They state that " in this report the word ' in ' has been used, but the possibility that the above (extracellular) theory is correct has not been overlooked "

From the evidence available it is seen that the relation of the plasmodium to its host cell at various stages of its development, still remains doubtful A more exact knowledge of the physical structure of normal and parasitized erythrocytes would help to explain the various observations mentioned above A renewed study of the migration of *P vivax* should be made under fresh conditions in a moist chamber on a warm stage or in a hot room

HAVE WE A PROPER PICTURE OF THE CYTOLOGICAL STRUCTURE OF THE MALARIA PARASITE?

The earliest work on the structure of the malaria parasite was carried out in fresh preparations Since the advent of the Romanowsky stains half a century ago, few other methods of examination of malarial blood have been used

These stains produce a beautiful picture of the plasmodia They form the most reliable method of diagnosis Unfortunately, this method of dry fixation and staining gives very varied results It is not, therefore, recognized by most protozoologists as producing a reliable picture of the minuter and more complicated features of the cytological structure of most protozoa* So much use has been made of this method of staining that the more reliable cytological method of wet fixation and iron hæmotoxylin coloration (Sinton and Mulligan, 1930) has been neglected We have none of the very careful descriptions of the plasmodia as have been given by Wenyon and by Dobell in the study of the intestinal amœbæ

*As Dobell once said— The day is now past when one can go into the field with a bottle of Giemsa and hope to rival Schaudinn ' This was also emphasized by an Editorial in the *Lancet* (1926)

Until this is done there will still remain many of the doubtful questions such as those detailed below It is suggested that, on account of its slow growth and the presence of all stages of its schizogonic cycle in the peripheral blood, *P inui* would form a most suitable subject for a study of this nature

WHAT IS THE NATURE OF THE VACUOLE SEEN IN THE RING FORMS OF THE MALARIA PARASITES?

Grassi and Feletti (1890) describe the vacuole as a large clear bladder-like nucleus with a delicate, often invisible, nuclear membrane and a nucleolus (the chromatin) [illegible]
by such older [illegible]
until the stud[illegible]
that the vacuole was formed inside the ring of protoplasm to give the young parasites [illegible]

[illegible] subject of the vacuole It states—
"The nature (i e, whether nuclear or nutritive) of the 'vacuole' seen in the ring forms is still uncertain, so that provisionally the best term appears to be vacuole" (Covell, Russell and Swellengrebel, 1953) *

Not all modern malariologists appear to be in doubt as to the nature of the vacuole For example, Le Dantec (1924) and many other workers describe the nucleus as vesicular with a karyosome, Boyd (1935) speaks of the nucleus of *P vivax* as round or oval with a limiting membrane, within which is a karyosome formed of one or an agglomeration of many chromatin granules, and Thomson (1932) stated that the nuclear structure of a *falciparum* gametocyte is a definite vesicular one

While there is little doubt that the 'vacuole' with its chromatin mass is a definite vesicular nucleus, further work with more precise cytological methods is needed to confirm this A few trials made on *P vivax* with the iron hæmotoxylin method of Sinton and Mulligan (1930), gave results which made the vacuole resemble very closely the limax type of vesicular nucleus seen with some intestinal amœbæ

The absence of a vacuole is usually given as one of the diagnostic characters of the early stages of gametocyte growth A careful study of these forms shows that the vacuole is still there but that the chromatin is evenly scattered through it, so obscuring its usual empty bladder like appearance

The chromatin has a very close connection with the vacuole In *P inui* with its slow rate of growth this is very well seen at all stages (*vide* Sinton, 1934, Plates III and IV)

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*Ewing in 1898 and later Rowley Lawson considered the vacuole as a small portion of the erythrocyte surrounded by two pseudopodia coalescing at their ends

WHAT ARE THE CYTOLOGICAL CHANGES WHICH OCCUR WHEN THE MALARIA PARASITE SEGMENTS?

Few workers appear to have studied the details of the schizogony of plasmodia using well recognized cytological methods Schaudinn (1902) described a sort of primitive mitosis in the asexual forms of *P vivax* In the same parasite, Ivanic (1937) described a form of promitosis going on to true mitosis in the later stages of schizogonous division More recently Wolcott (1954) has studied the nuclear structure and division of *P vivax* He says that he never found the vesicular nucleus and karyosome reported by Ivanic (1937) However, he describes a mitotic stage in the cycle of schizogony with two chromosomes and a well marked achromatic spindle He used wet films stained with Giemsa, so his observations require confirmation by more precise cytological methods

Here again the slow rate of growth of *P inui* and the abundance of all stages in the peripheral blood, should make this species an admirable one for the study of nuclear division The early stages of chromatin division and their relation to the vacuole are shown in Plate VI, Fig 25-28 At this stage of schizogony the findings suggest simple binary fission of a vesicular nucleus

IS MULTIPLE INFESTATION OF ERYTHROCYTES IN MALIGNANT TERTIAN INFECTIONS DUE TO PREMATURE DIVISION OF YOUNG SCHIZONTS?

In very severe infection of *falciparum* malaria, it is not uncommon to find some red cells infested with many parasites, even as many as six per cell (Plate VI, Fig 24)

Some workers suggest that this is due to binary fission of the young schizonts and not to the attack of the cell by several merozoites (Alessandrini, 1933)

Schuffner and de Graaf (1937) have discussed this hypothesis and come to the conclusion that this multiplicity of infestation was due to the greater attraction afforded by certain erythrocytes to the young parasites Hingst (1934 1938), however, attributes such multiple infections as due to amitotic division of young schizonts already infesting the cell rather than to multiple invasion of single merozoites

DOES THE METHOD OF PREPARATION CHANGE THE *MORPHOLOGICAL* CHARACTERS OF THE PARASITE?

Sinton (1955) has discussed the causation of 'banded' forms in infections with *P malariæ* and *P inui* He has produced reasons to support the view that these are not found *in vivo*, but are distortions produced by the method of preparation of the thin film They give indications of the physical condition of the parasite at the time that the film was made They are valuable aids in diagnosis Similarly with *P tenue* the characteristic forms seen appear to be produced in a similar manner (Callanan, 1926) They indicate a special physical state of the plasmodium at the time This shows a tertian periodicity

WHAT IS THE NATURE OF THE CHANGES IN THE ERYTHROCYTES INFESTED BY MALARIA PARASITES?

WHAT CAUSES THE CHANGES IN THE SIZE AND SHAPE OF INFESTED ERYTHROCYTES?

The enlargement of the infested red cell in *vivax* infections is well known On the other hand, the æstivo autumnal parasite in its later stages is found more commonly with a smaller cell, which may show marked colour changes when examined in the fresh We have still to discover the different causations of these changes

The oval and fimbriated erythrocytes, which are seen in thin films of the [illegible] h *P ovale* and *P knowlesi*, are often of [illegible] .) has discussed the probable causation [illegible] *in vivo* but are produced mechanically during the preparation of thin films which dry very quickly, they indicate a special physical character of the cells

WHAT IS THE CAUSE OF THE DIFFERENT TYPES OF "STIPPLING" SEEN IN ERYTHROCYTES INFESTED BY DIFFERENT SPECIES OF PLASMODIUM?

Schuffner (1899) was the first to describe these changes He considered that the Schuffner's dots of *vivax* infections were due to degenerate particles in the stroma of the infested red cells

These changes were examined in some detail by Maurer (1901, 1902), who gave the same reason as Schuffner for the stippling seen in *vivax* infections In the case of the " red-coloured dots, little rings and lines " with the *Laverania* species (Maurer's dots), he concludes that these were due to changes or losses of substance on the upper surface of the erythrocytes, which are the result of the attacks made by the parasite in order to adhere to its host cell and to obtain nourishment " The numbers are said to increase with the size of the parasite and are not stationary as with *vivax* stippling

Billet [illegible]

agree [illegible]

mechan [illegible]

the thr [illegible]

pseudopodia to some of these spots, which he believes are either a secretion of the parasite or a little of its own substance The number of the dots is thought to be a function of the amœboid activity of the parasite species

The exact nature of these markings is still in doubt In addition to the [illegible] es described [illegible] ria These [illegible] bodies and a dark red deposit around segmenting forms is reported and discussed by Sinton and Mulligan (1933*b*), Sinton (1934), and Mulligan (1935) in all three species of oriental simian plasmodia Malamos (1934) found a capsule with *P vivax*, *P ovale* and *P knowlesi* Garnham (1931) and Thomson (1933) investigated curious bodies seen in red cells with immature gametocytes of *P falciparum*.

Stippling and similar changes have been seen in infections with most kinds of malaria infection * The demonstration of these markings depends very largely upon the type and intensity of the stain used The use of alkaline distilled water,

In the same category of changes comes the "capsule" which is sometimes so conspicuous around deeply stained crescents This is discussed by Garnham (1931, 1933) and Thomson and Robertson (1932) Warasi (1932) thinks that the parasite is covered by two membranes, first the periplast of the red cell and second the periplast of the parasite Between these two is the hæmoglobin, and as the parasite grows, this disappears and the two membranes fuse together to form a capsule Apart from this, Mannaberg (1894) states that in fresh preparations a perfectly recognisable double capsule is seen

Many of the appearances seen support the idea of Schuffner (1899) that the *origin of Schuffner's dots is different from Maurer's ones The latter look as if* they were produced directly by the parasite and were not merely due to degenerative changes in the erythrocyte

ARE MORE THAN ONE SPECIES OF PARASITE INCLUDED UNDER THE NAME OF "*PLASMODIUM FALCIPARUM*?

Even from the earliest days of the separation of the crescent-forming parasites from the quartan and tertian ones, there has been doubt as to how many species of parasite were included in the former category These were first divided by the supposed periodicity of their febrile paroxysms Later morphological differences were described as well as variations in their febrile reactions, in the effects of *treatment, and in their susceptibilities to infecting the same insect host*

WHAT IS THE DURATION OF THE ERYTHROCYTIC CYCLE OF SCHIZOGONY OF THE ÆSTIVO AUTUMNAL MALARIA PARASITES?

The earlier workers on the malaria parasites, such as Marchiafava, Bignami and Grassi considered that there were two kinds of æstivo autumnal parasites—a tertian one and a quotidian Mannaberg (1894) divided them into a tertian and two quotidians Even as late as 1914, Manson following the last worker grouped them as (*a*) Subtertian due to *Laverania malariæ* (*syn P falciparum*), (*b*) Pigmented quotidian due to *P præcox*, and (*c*) unpigmented quotidian due to *L immaculata*

The fever curve in these infections is very often remittent, not intermittent, so that they may appear to have a quotidian periodicity In recent years all these forms have been grouped as "malignant *tertian*", and the absence of tertian febrile periodicity explained as due to the schizogony of all the parasites not being simultaneous but distributed over several hours Why such an abnormal schizogony

*The dots seen in quartan malaria are often called Ziemann's but Seyfarth (1924) mentions them as Brug's

should occur in this species of malaria parasite and not in the other three infecting man, seems curious, unless this is another difference possessed by the genus *Laverania* as compared with the genus *Plasmodium*

Even although the term 'malignant tertian' is now used by most English writers, there still seems to be great doubt as to the duration of the cycle of erythrocytic schizogony Various authors give this as 24 28 hours, 36-40 hours [illegible] he [illegible] be

The prolongation of the febrile paroxysm in these supposedly tertian infections could be accounted for by a double infection, such as gives rise to quotidian periodicity in some [illegible] infections It is possible, however, that the older workers were correct, and that a true quotidian species occurs as in the case of *P knowlesi* in simian malaria Indeed, Craig (1909, 1921) has reported such a parasite, which he named *P falciparum quotidianum* Row (1917) also describes and pictures the parasites seen in a culture of 'quotidian malaria' (*Laverania præcox*)

One needs more careful study along the lines used by Sinton (1934) and Mulligan (1935) to determine the duration of the cycles in the species of monkey malaria Sinton (1922) using this method showed that *P tenue* had a definite tertian periodicity Cultural methods might also be useful The strains used would be more easily studied under conditions of malaria therapy It is suggested that possibly strains from the North-West of India should be compared with those from the Eastern parts, and African ones with Italian

From this it is seen that the question still remains unsolved as to whether all 'malignant tertian' parasites have a true tertian periodicity, i e, are only one species.

CAN SEVERAL SPECIES OF ÆSTIVO-AUTUMNAL MALARIA PARASITES BE SEPARATED BY THEIR MORPHOLOGICAL CHARACTERS?

While the older writers separated their different species of the *Laverania* [illegible]

The sinking of all these crescent forming plasmodia in one species—*P. falciparum* (*P. præcox*, *P immaculatum*)—seemed to settle the question, but in more recent years many workers have doubted the unity of this species For example, Ross (1911) was still inclined to believe that there are two or three species in this group, O Gorman-Lalor (1913) reported the unusual morphology of such parasites in a blackwater-fever area in India, Marchoux (1922) points out differences between African, Italian and Macedonian forms, Schuffner and Hylkema (1922) reported what they thought was a special form during an epidemic at Belwan in Sumatra, many other workers are also doubtful

The American worker, Craig (1909,1921) describes what he considers to be a new variety of *P falciparum* which he has named *P falciparum quotidianum*

Grave doubt has been cast by many workers on the unicity of the Italian and the African forms of *P falciparum* Ziemann (1915) thought that the form found in the Cameroons, West Africa, was so different from the Italian form that he named it *P perniciosum*, and has since described it in comparison with other forms of *P falciparum* (Ziemann, 1938)

James and Kauntze (1930) considered that the malignant tertian parasite seen by them in East Africa differed from the classical description of *P falciparum* Many Italian workers noted differences between the Italian parasite and some found in Abyssinia The latter parasite has been named by Giovannola (1938) as *P falciparum æthiopicum*

A curious type of *P falciparum* was found by Marzinowsky (1916) in South Russia, which showed segmenting forms in the peripheral blood This he named *P caucasicum* *

The species most in dispute has been *P tenue*, described by Stephens (1914) from specimens received from the old Central Provinces in India, and later from West Africa (Stephens, 1915)

Sinton (1922) carefully examined five cases from Nagpur Jail, and was convinced that this was a separate species of malignant tertian parasite Since then other data have been collected to support this conclusion

In the Indian sub continent there seem to be at least two morphological species of *Laverania*—(*i*) the ordinary classical form, only seen with small rings in the peripheral blood (except in pernicious cases), occurring commonly in the north western parts of the country, and (*ii*) the large-ringed form (small rings may sometimes be detected in the very early stages) common in the eastern and southern parts of the country It is the latter parasite which shows a "tenue" stage † Every year blood films taken from cases in the latter parts of India, were given to the post graduate students in our Annual Malaria Class Students from the northwestern areas almost invariably diagnosed these initially as *P vivax*,

extreme rarity there, while they are relatively common in those from some of the eastern parts of this sub continent (Sinton, 1927)

Apart from the 'tenue' stage with its tertian periodicity, the parasite is seen for a longer time in the peripheral blood, even as late as 36th hour of its cycle, and the rings are much larger than the classical *P falciparum* The pigment sometimes

* In the winter of 1934-35 some slides were sent me from Gilgit in Kashmir showing parasites resembling those described by Marzinowsky (1916) *Unfortunately the specimens were mislaid before a full investigation could be made*

...phological characteristic of this parasite
the method of prepar
e parasite at one stage
een found in the cycle
an earlier point in its
cycle

seen in the largest rings is finer, more scattered and lighter in colour than the coarser dark brown or jet-black masses seen in *P falciparum* at a similar stage The golden yellow colour of this pigment was well seen in the only mature schizont (Plate VI, Fig 23) observed in Sinton's cases, and which contained eight merozoites (*cf* Marchoux, 1926) The Maurer's dots seen in the classical *P falciparum* are usually described as irregular in shape and few in number, and as often being difficult to demonstrate In *P tenue* they stain more easily, and are more numerous, rounded, linear and coccoid in shape (Plate VI, Fig 22)

These forms have been reported by workers in many other tropical countries, for example Hucks and Bowden (1924) and Darling (1925) in the United States, Perekropoff (1917) in Russia, Sergent *et al* (1913) and Vialatte (1922) in North Africa, and Jerace (1932) in Italy, among a host of others I have received beautiful slides of this form sent by Dr G Fraser from Assam and Dr K L Rustomjee from Ceylon Russell (1928) gives a careful review of the literature up to that date

Is the small ring form that of areas of sea on l and or dem ...

and Mulligan (1933*a*,1933*b*) were unable in the cases of *P knowlesi* and *P cynomolgi* to find that such conditions caused any morphological changes in the character of these parasites

In spite of the evidence produced, the latest authoritative statement says—"*P tenue* Stephens, 1914, is no longer accepted as a distinct species" (Covell *et al*, 1953)

If *P tenue* be accepted as a true species what is its proper specific name? The parasite is probably the same as one of those originally described as either *P præcox* or *P immaculatum* As pointed out by Christophers and Sinton (1938) both these names are invalid as having first been used to designate avian parasites Similarly, the specific name *tenue* is also invalid, because a few months before Stephens (1914) used it, a parasite of the Peking nightingale had been named *Hæmamœba tenuis* by Laveran and Marullax (1914) Ziemann (1915), in his discussion of the human parasites, names it in his description of the figures given on his plate—"*Plasmodium khartunense* (From Khartoum) Synonym *Plasmodium tenue* Stephens"

ARE THERE CLINICALLY DIFFERENT 'STRAINS' OF THE ÆSTIVO AUTUMNAL PARASITE?

Apart from the question of the periodicity of the febrile paroxysms, other distinct clinical differences have been reported between 'malignant tertian' infections in various parts of the world

When James (1932) compared the Rome strain of *P falciparum* with an Indian one, he found that it needed almost ten times the dosage of quinine to control the former infection, which was, however, easily affected by atebrin In the Panama, very heavy doses of quinine, as compared with European practice, are required to reduce pyrexia Fairley (1946) has reported that almost double

the normal dosage of atebrin was necessary to suppress some *falciparum* infections in the Aitepe-Wewak area of New Guinea Other workers in describing their new species have noted clinical differences

O'Gorman Lalor (1913) and Hassal-Wright (1920) drew attention to unusual forms of the parasite found in blackwater-fever areas of India Sinton (1927) remarked upon the similarity of the recorded distribution of *P tenue* and the same syndrome Cort (1929) noted a special form of subtertian parasite in association with hæmoglob
a relationship between *P*
in drawing attention to th
text book descriptions, conclude that " the subject certainly merits careful enquiry in Kenya and Uganda, particularly in districts where blackwater fever occurs "

FAILURE TO INFECT SOME ANOPHELINES WITH FOREIGN STRAINS OF *P FALCIPARUM*

James, Nicol and Shute (1932) found great difficulty in getting any infections in *A maculipennis* var *atroparvus* with Indian strains of *P falciparum* as compared with the Rome one, although clinically the latter was more pathogenic to man This was confirmed by Shute (1940) with other strains of tropical origin

Raffaele and Lega (1937) remark upon the difficulty of infecting *A maculipennis* with their new variety, *P falciparum aethiopicum* Similar results with both *P falciparum* and *P vivax* have been recorded in America

As we do not know what are the factors which govern the susceptibility of mosquitoes to any malarial infection, it is not possible to decide whether these failures are due to something in the insect or something in the parasite, either of a strain or a specific character

WHAT IS THE FATE OF THE SPOROZOITES IN THE INSECT HOST?

Ross (1905) in describing his original discovery said—" I saw the thread like bodies, although apparently without motion themselves, were soon scattered by the insect's circulation all through its body '. This passive distribution was also noted by Grassi and Schaudinn Muhlens (1921, 1931) showed that the sporozoites could be found in the muscles and even in the legs and in the appendages of the head

The concentration of these forms in the salivary glands is great, but it is uncertain whether this is due to chemiotaxis or purely a matter of chance (Schaudinn ,1902) It is easy to understand how the sporozoites in the salivary glands are got rid of in the acts of biting, but the fate of the others is still uncertain

In the early stages of the infection, at least, if a piece of a segment of a leg is severed from an infective living insect and the fluid expressed from it, this is found to contain large numbers of sporozoites What is the ultimate fate of these? Are they infective? Do they form a reservoir from which the supply in the glands is replenished as these become depleted by biting? How long can they be detected and are the insects still infective after they disappear from the appendages?

Schuffner, Korteweg and Swellengrebel (1929) found that in the autumn the bites of one or two mosquitoes failed to cause malaria in the usual incubation period, but infection appeared after eight to nine months The impression formed by me while working in the Malaria Laboratory at Horton was that, with the Roumanian strain of *P vivax*, these prolonged incubations occurred more often when the sporozoites had been present for several weeks in the insect host Were these latent infections caused by sporozoites which had been a long time in other parts of the insect's body? Did this give rise to senility of these parasites or was it merely a smaller dose of infection that was injected?

WHY ARE SOME SPECIES OF ANOPHELINES SUSCEPTIBLE TO HUMAN MALARIAL INFECTIONS WHILE OTHERS ARE NOT?

It is well known that the gametocytes of all the human species of *Plasmodium* will become gametes and conjugate to form zygotes, when taken into the stomach of even culicine mosquitoes These zygotes never develop further in culicines and only in certain species of anophelines As mentioned above the zygotes of some strains of parasite may behave in a refractory manner in anophelines which are normally susceptible to such infection of other strains

Why this occurs has never been determined Is it due to some factor in the insect or some in the parasite? The best researches on the subject have been those of Huff (1934), but even these have failed to give a satisfactory explanation

MISCELLANEOUS QUESTIONS

(i) WHAT IS THE MALARIA 'TOXIN' AND WHAT IS THE CAUSE OF THE MALARIA PAROXYSM?

Is there no true malaria toxin? Is the paroxysm due to a condition of anaphylactoid shock caused by the discharge into the blood stream of particles of pigment, remains of parasitized blood cells, and pieces of parasite at the moment of schizogony (Sinton *et al*, 1928)?

(ii) CAN DIFFERENT IMMUNOLOGICAL STRAINS OF PARASITE BE DIFFERENTIATED BY DERMAL OR BY SEROLOGICAL TESTS?

Sinton and Mulligan (1932) showed that an antigen prepared from an almost pure suspension of *P knowlesi* produced a marked dermal reaction with animals infected with a similar parasite Could this method be used to differentiate the different strains of this parasite?

Before it became possible to isolate large quantities of parasite substance (Sinton and Mulligan, 1932), many experiments were made to perfect a complement fixation test Could a better antigen now be produced which would give a differential diagnosis, between the species or even the strains of monkey malaria?

Several precipitin tests have been tried for malarial infection The results in these appear to depend merely upon their effects upon the increased globulin content of the blood, and as such are poor diagnostically

(iii) WHAT IS THE NATURE OF THE ANTIBODIES IN MALARIA?

From a study of malarial immunity it is evident that two factors are involved—an anti parasitic one and an anti toxic one (Sinton 1939) The former acts by a destruction of the parasites and the latter by neutralizing their effects

Is the anti parasitic one a lysin which renders the parasites more readily destroyed by the macrophages or is it an opsonin which causes the macrophages to attack the parasites with greater avidity?

While we have no information as to the nature of the anti toxic one, we can only consider its results

Does it pass through the placenta and so cause a passive immunity in the fœtus or does the latter produce its own antibodies under the stimulation of malarial 'toxin' entering its circulation from the blood of its mother (Sinton 1939*a*)? Can acquired maternal immunity be transmitted through her milk?

(iv) WHAT IS THE ORIGIN OF THE GAMETOCYTES?

Are these derived from special exoerythrocytic merozoites or from the blood ones? Probably at least from the latter, as they occur after blood inoculations

At what stage of their development do these forms take on their sexual character, or are they so *ab initio*? Do they have an intracellular position as compared with asexual forms, and if so would this determine their fate? Does the environment in which they develop have any effect upon their fate, *i e*, do the special conditions of the spleen and bone marrow have any action in determining their development into sexual forms?

(v) WHAT SPECIES OF PLASMODIUM OCCUR IN THE LOWER MONKEYS OF AFRICA?

Sinton and Mulligan (1932*a* 1933), Mulligan (1935) and Sinton (1934) made a careful study of the malaria parasites of the lower monkeys of the Old World

Those from Asian countries were found to be infected with at least three distinct species—(*a*) *P knowlesi* Sinton and Mulligan, 1932, having a 24 hour cycle of schizogony in the erythrocytes (*b*) *P cynomolgi* Mayer, 1907, with a 48 hour cycle, and (*c*) *P inui* Halberstadter and Prowazek, 1907, with a 72 hour cycle Among the lower African monkeys, *P gonderi* Sinton and Mulligan, 1932 (vel *P kochi* Gonder and Berenberg Gossler, 1908) and *P kochi* Laveran, 1899, with varieties were described The latter parasite has since been found not to be a *Plasmodium* but to belong to the genus *Hepatocystis*

Except for the careful studies made by Gonder and Berenberg Gossler (1908), Berenberg Gossler (1909) and Gonder and Rodenwaldt (1910), the plasmodial parasites of the lower African monkeys seem to have had little attention Is *P gonderi* identical with *P cynomolgi*? How many African species are there?

SUMMARY

It is pointed out that there are many unsolved problems in our knowledge of malaria parasites and these are discussed

1 Should genus *Laverania* be again separated from the genus *Plasmodium*?

2 Is the malaria parasite inside or outside the host erythrocyte?

3 Have we a proper picture of the cytological structure of the malaria parasite?

(*a*) What is the nature of the 'vacuole'?

(*b*) What cytological changes occur when the parasite segments?

(*c*) Are multiple infections of the red cells due to simple binary fission and not to invasion by multiple parasites?

(*d*) Is the morphological appearance of the parasite in thin films influenced by the method of preparation?

4 What is the nature of the changes in parasitized erythrocytes?

5 Does the present species '*P falciparum*' contain more than one species?

(*a*) What is the duration of the cycle of schizogony?

(*b*) Can several species be separated by their morphology?

(*c*) Do the infections caused by these species vary clinically?

(*d*) Do they vary in their ability to infect anophelines?

6 What is the fate of the sporozoites in the insect host?

7 Why are some species of anophelines susceptible to malarial infection while others are not?

8 Miscellaneous questions

(*a*) Is there a malaria 'toxin'?

(*b*) Can different immunological strains be separated by laboratory tests?

(*c*) What is the nature of the 'antibodies' in malaria?

(*d*) What is the origin of the gametocytes?

(*e*) What species of *Plasmodium* occur in the lower monkeys of Africa?

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SOME EVOLUTIONARY POSSIBILITIES IN THE HISTORY OF THE MALARIA PARASITES

BY

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[July 28 1955]

THE problem of the evolution of the malaria parasites is, in the nature of things, one which can never be wholly solved but its very difficulty makes it the more challenging to the medical men and to the biologist It is a question which has puzzled malariologists almost ever since the causative organisms of malaria were discovered, some 75 years ago, and perhaps we are even now not much nearer a solution Yet so much new light has been shed on what may be called the natural history of malaria in the past decade or two, that it is worthwhile taking a new look at the problem

Involved, of course, are not only the parasites themselves, but their hosts, both vertebrate and invertebrate stay when biological relationships are gree of kinship of existing species of to tell us little of what we might call the third dimension of the problem, or time And the ancestral relationships are those in which are we most interested From what did the malaria parasites evolve? What may have been their earlier hosts? What light, if any, can be thrown on the evolutionary development of the complex life cycle of this genus of parasites?

The best evidence for the evolutionary history of any living thing is undoubtedly that afforded by fossils, but fossil malaria parasites are, of course, non-existent, as indeed are fossil remains of most other parasitic organisms Yet fossil Foraminifera are known from Cambrian times (some 500 million years ago), and Radiolaria may be even older, having been reported from rocks of pre-Cambrian age (Chapman, 1902, Pirsson and Schuchert, 1924, Glaessner, 1945) Both groups of Protozoa are free living, and both are almost exclusively marine, and their antiquity is therefore, only of interest here because it shows the great age of the phylum, but it suggests that the parasitic protozoa may also have had a very long evolutionary history

Indeed, it may safely be assumed that there were protozoa of at least the two orders just mentioned long before the oldest of these fossils were laid down, for the morphology of many of the latter is much like that of contemporary forms, and it is, therefore, probable that their life-histories were also similar Since the life-cycles of the relatively few of these organisms which have been thoroughly studied are complex, including the production of gametes and fertilization evolution must have already gone a very long way even in pre-Cambrian times It seems likely that life-cycles as complex as those exhibited by such parasites as the malaria plasmodia were even then commonplace

Additional evidence that this was probably the case is furnished by the occurrence of fossil algæ in rocks of this age. Algæ are closely *related to the plant*

milar life cycles, also
tes are also known
perhaps 140,000,000
years ago Ciliophora and Sporozoa are unknown in the fossil state, although since some of the former have skeletons or tests it is not impossible that such remains may eventually be found

Of course, one must suppose that free living organisms antedated those of parasitic habit, an(

living ancestors
Sandon (1932) rer
some unicellular organisms, previously accustomed to nourishing themselves after the manner of plants, began to eat the bodies (either living or dead) of their neighbours" Some parasitic protozoa are perhaps, even now, not far removed from that stage, since they closely resemble free-living species But the Sporozoa, all of which are parasites, resemble no free living protozoa known to day, and as the great protozoologist, Gary N Calkins, used to say in his lectures many years ago, they represent a group the members of which are so different that it is often impossible even to suppose any mutual relationship Thus, however ancient some of the free-living protozoa may be, we have no direct evidence bearing on the

The malaria parasites are classified as Hæmosporidia, subclass of the Telosporidia This subclass contains two families which are certainly very closely related the Hæmoproteidæ and the Plasmodiidæ, to the second of which belong the malaria parasites Both families are large as far as the number of species is concerned, but small in the number of genera contained There are at least 50 recognized species of *Plasmodium*, the only genus of the Plasmodiidæ, and probably many more species of *Leucocytozoon* and *Haemoproteus* (the two genera comprising the Hæmoproteidæ)

The second order in the class Hæmosporidia contains only the single family Babesiidæ, together with two genera of doubtful status *Dactylosoma* and *Toxoplasma**

* According to the classification of Hall (1953)

The Babesias are parasites of red cells, and superficially resemble the malaria plasmodia, but although they are incompletely known, the two orders do not appear to be closely related Both vectors and life-cycles differ considerably

It has long been thought that the malaria parasites may have originated from the coccidia Mesnil (1899) seems to have been the first to point this out, and the view was supported by Schaudinn (1899), and later by Reichenow (1912) Wenyon (1926) spoke of the affinities existing between coccidia and the hæmosporidia, from the first of which the second group " may be supposed to have evolved "

The evidence for the belief that the malaria plasmodia (and presumably also their close relatives, the genera *Hæmoproteus* and *Leucocytozoon*) arose from the coccidia, lies in the close similarity of their life cycles All of these organisms are typically cell parasites, and all exhibit sexual stages The coccidia are generally parasites of the intestinal epithelium, in the cells of which they undergo a number of asexual generations, culminating in the production of gametes After fertilization, the zygote develops into a resistant oocyst, containing sporocysts which in turn contain sporozoites These constitute the infective stages, and initiate a new infection after ingestion by a fresh host There is no vector (but sometimes an alternation of hosts), and hence resistant stages are generally necessary for survival without the host

The life cycles of the malaria parasites are obviously very similar to this pattern, the chief differences being the addition of a second host which, in all species where the life-histories have been completely studied, is a mosquito, and the lack of a resistant oocyst stage The fact that the parasites reside in the erythrocytes of the vertebrate host, rather than in the intestinal epithelium, seems of much less significance than it did before the exoerythrocytic stages of the cycle were discovered two decades ago

The chief controversy revolves around the question of whether the ancestral organisms from which the Plasmodiidæ evolved were parasites of invertebrates, and therefore presumably of biting flies (such as mosquitoes, hippoboscids, *Simulium*, and others), or of the vertebrates And if it is conceded that this family may first have been parasites of vertebrates, were their hosts in the beginning perhaps reptiles, since it was from the latter class that both birds and mammals evolved?

These problems are [illegible]

do not occur in insect hosts

The fact that most coccidia are parasites of the gut suggests that they were originally acquired as the result of ingesting food or water contaminated with them Of course, the forms from which they evolved must once have been free-living, although it is at least conceivable that they may have parasitized invertebrates before becoming adapted to life in veretbrate hosts, and that the latter were first infected by ingesting the former In any case, it seems probable that these ancestors of the coccidia of vertebrates had already developed a highly complex life-cycle,

just as those protozoa we know as fossils must have done Doubtless cysts, the production of which often climaxes a period of asexual reproduction and may also involve a sexual cycle, were the infective stage Certainly a good deal of adaptation must have been required for life within a living host, but protozoan cysts have often been observed to survive passage through the intestine and some free-living species may even persist there for a limited time

Huff (1938, 1945) has urged the point of view that the malaria plasmodia and their close relatives were at first parasites of insects, and became secondarily adapted to life in vertebrates after their insect hosts developed the blood sucking habit The fact that these parasites do not seem to be pathogenic to their vectors favours this theory, and yet, as Ball (1943) has rather convincingly maintained there are too many exceptions to the rule that the degree of pathogenicity is inversely related to the duration of association between host and parasite to make this type of evidence more than doubtfully suggestive

Huff also emphasizes the fact that the life cycles of the Hæmoproteidæ and Plasmodiidæ are more similar as far as the insect host is concerned than for the vertebrate host This is true (although we still know little or nothing of the life histories of many species), but it is worth pointing out that the newer knowledge of the vertebrate portions of these life cycles makes them seem ever more alike

The known insect hosts of the Hæmoproteidæ and Plasmodiidæ include hippoboscid flies (*Hæmoproteus*), *Simulium* (*Leucocytozoon*), and mosquitoes (*Plasmodium*) The first of these vector groups is only distantly related to the last two, and it may (as Huff concedes) suggest—despite the undoubted similarity of the insect portions of the life cycles of all three genera of blood parasites—that this portion of the cycle developed later than that in the vertebrate host

But, in any case, the insect vertebrate type of life cycle characteristic of [illegible] olved before the ancestors of the present [illegible] That this dietary requirement may [illegible] the fact that it is, even today, restricted to females As for the antiquity of mosquitoes, sufficiently like those of today to be recognizable as such they are known from Eocene times, some 60 million years ago A fossil form, believed to be a male mosquito (note the plume-like antennæ), found by the writer in the famous Oligocene shales of Florissant, Colorado is shown in Plate VII, Fig 1 Mosquitoes are, of course older than this, and doubtless this is also true of other blood sucking Diptera Diptera as a group appeared as early as the middle Jurassic, but they were at first restricted to midges and cranefly like forms (Carpenter, 1953) The oldest known fossil insects (notably the extinct Palæodictyoptera and cockroaches) were extant in the later Carboniferous period, which is believed to have been about 250 million years ago It is worth noting that insect evolution had gone a long way even then, and it is very likely that insects were already well supplied with protozoan and other parasites

The classes of vertebrates to which the known natural hosts of the malaria plasmodia belong include, as perhaps we should expect, all those of terrestrial habitat * But susceptible host species are not evenly distributed among these classes,

*Malaria parasites have also been reported from the bull frog by Fantham Porter and Richardson (1942) but nothing else is known about them









Fi s 1 A fossil mosquito (male) from the famous Ol gocene shales of Florissant Colorado (Note the

2

3

4

nor are such species relatively numerous Most of the known reptilian host species of plasmodia are lizards, and the majority of avian hosts are passerines There is much more variety among the malaria-susceptible species of mammals

The striking parallelism between the reptilian and avian species of *Plasmodium* has often been noted Together these species constitute almost two-thirds of the recognized species of the genus Unfortunately very little is yet known about the life cycles of the malaria parasites of reptiles, but the resemblances in morphology of the avian and reptilian types point to a close relationship It may be that such similarities are to be explained as due to parallel evolution, but it seems more likely to be the result of relatively slow evolutionary change on the part of the parasites since the original separation of avian and reptilian stocks, even though bird and lizard lines of descent must have diverged at a very early period

The relatively small number of malaria susceptible species among the mammals, and their spotty taxonomic distribution (antelopes, water buffalo, rodents, primates, bats, to mention the more important) seems to suggest that malaria among them was a kind of after-thought on the part of nature Perhaps the greater pathogenicity of some of the mammalian species of *Plasmodium* points to the same conclusion

Another fact which may support the belief that malaria was originally a disease of reptiles, and then also of birds, is the very common occurrence of the two closely related genera* of blood protozoa, *Hæmoproteus* and *Leucocytozoon*, among birds and, in the case of the former, among reptiles also As with the avian malarias, infections of *Hæmoproteus* and *Leucocytozoon* seem usually to affect the host very little, a fact which seems to indicate a very long period of host parasite association

Still another fact which is in accord with the possible earlier occurrence of [illegible] notremes, [illegible] reas birds [illegible] (Romer, [illegible] Diptera, and, especially, the blood sucking types now serving as vectors of malarial and malaria related parasites (But it must be remembered that the vectors of the great majority of species of *Plasmodium* are still unknown, and there is no certainty that all are mosquitoes It is also true that the vectors of most species of *Hæmoproteus* and *Leucocytozoon* still remain to be discovered)

The occurrence among the coccidia of genera such as *Shellackia* and *Lankesterella* (family Lankesterellidæ), in which a life-cycle not unlike that of the Hæmosporidia occurs, has often been regarded as supporting the theory that parasites of this group originated in vertebrate rather than invertebrate hosts Perhaps this is best regarded as simply the result of parallel evolution, but it certainly indicates that the original hosts of parasites such as these need not have been insects, for here the cycle involves in the one case (*Shellackia*) lizards and mites,

*There are also certain hæmatozoa of mam[illegible] that they were for a long time put into the gen[illegible] monkeys and certa n s m lar parasites of bats [illegible] perhaps be regarded as the mammalian analog[illegible] Hunt 1947, Garnham 1948 54 Manwell, 1948)

and in the other frogs and leeches The nature of the cells parasitized in the vertebrate hosts also certainly suggests that the coccidian ancestors of the Hæmosporidia may have developed along similar lines, for *Shellackia* multiplies in the intestinal epithelium of lizards, the sporozoites later entering erythrocytes, and *Lankesterella* reproduces in the endothelium of the capillaries of the frog, with subsequent sporozoite invasion of the red cells The tissue stages may be regarded as corresponding to the reproductive stages of *Hæmoproteus* and *Leucocytozoon* in the vertebrate, and to the exoerythrocytic forms in malaria

In the light of the occurrence of life cycles such as these among certain of the coccidia, it is rather tempting to think of *Hæmoproteus* as perhaps the oldest

(hippoboscids), presumably indicating a long period of evolution on their part, points to alike conclusion

Leucocytozoon may have originated later, and still seems to be confined to

ɔd cells
would

Little can be said as to the possible or probable mutual relationships of the different species of *Plasmodium* The life cycles of all, as far as is known, are similar, and follow a pattern similar to that in the genus *Hæmoproteus* and *Leucocytozoon* It might be thought that those avian and reptilian species of *Plasmodium* which most closely resemble one another arose the one from the other This may, of course, have been the case, but parallel evolution may also have occurred It is possible to divide species of the genus according to whether the gametocytes are elongate, or round or irregular, and according to the nature of

ɔne, the types are *Plasmodium gallinaceum*
um of reptiles exhibits both kinds of
and Huff, 1944) On the whole, although such characteristics afford convenient bases for classification, so little is yet known about the cycles of most species of *Plasmodium* (and this is equally true of species of *Hæmoproteus* and *Leucocytozoon*) that it does not now seem worthwhile to try to work out the detailed relationships of any of these parasites

*Fallis *et al* (1951) and Cook (1954) have shown that *Leucocytozoon simondi* may invade erythrocytes the writer has also observed this in other species occasionally

SUMMARY.

The problem of the evolution of the malaria parasites and their close relatives among the Hæmosporidia is considered, and it is suggested that they may well have arisen from coccidia of vertebrates rather than from those of insects, as has been more commonly supposed. This possibility is consistent with, or is supported by, various facts of palæontology and of host-parasite relationships But too little is known about the life-cycles and physiology of many species of the Hæmosporidia to give anything like a final answer to the problem of their evolution.

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ABSENCE OF CROSS-IMMUNITY BETWEEN *PLASMODIUM CYNOMOLGI* AND *PLASMODIUM GONDERI*.

BY

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(July 21, 1955)

THREE species of *vivax* like malaria parasites are known to occur in lower monkeys *Plasmodium cynomolgi* (Mayer, 1907) in oriental macaques (chiefly from Malaya), *P gonderi* (Rodhain and van den Berghe, 1936) in African mangabeys (chiefly from Belgian Congo) and *P simium* (Fonseca, 1951) in Brazilian spider monkeys All three species are much alike they exhibit a tertian periodicity in the blood, cause enlargement of the erythrocyte accompanied by Schuffner's stippling, and morphologically resemble *P vivax* in the asexual and sexual stages When Sinton and Mulligan (1933) tried to disentangle the muddled systematics

var *gonderi*

and they

Rodhain

ts cycle in

the blood occupied 48 hours and that it could, therefore, hardly be called a sub-

never been isolated, from the descriptions given by Fonseca (1951), this South American representative of simian benign tertian malaria parasite has no features distinguishing it from other members of the group

Strains of malaria parasites behave differently in their immunity reactions Avian species as a whole have a wide spectrum of immunity, the larger species

et al., 1955), so-called strains of *P. falciparum* and *P. vivax* are so different (immunologically and in other ways) that they sometimes receive sub-specific names. Rodhain (1954) has recently used the absence of cross-immunity between *P. bergl* and *P. vinckei* as confirmation that they represent distinct species.

We felt that it would be useful to discover if cross-immunity tests woul give a clue to the specific status of *P. cynomolgi* and *P. gonderi*. We possessed number of monkeys highly immune to the former, and thus had a good opportunity of carrying out the requisite experiments

IMMUNIZATION OF MONKEYS.

Four *Macaca mulatta* (Numbers 81, 99, 101, 102) were immunized against *P. cynomolgi** by blood and sporozoite infections as shown in Table I.

TABLE I

Immunization of monkeys against P. cynomolgi.

Monkey Number	Date of first infection with *P. cynomolgi*	Mode of first infection	Superinfection with *P. cynomolgi*: Date of super infection	Mode of super-infection	Subsequent course of infection
81	May 29, 1951	Sporozoites	14/5/53 24/8/53 28/7/54 2/2/55	Blood Blood Sporozoites Blood	* ‡ ‡ ‡ †
99	April 25 1952	Sporozoites	14/5/53 24/8/53 28/7/54 2/2/55 25/2/55	Blood Blood Sporozoites Blood Sporozoites	† † ‡ ‡ ‡ †
101	July 23, 1952	Blood	14/5/53 24/8/53 28/7/54 2/2/55	Blood Blood Sporozoites Blood	‡ ‡ ‡ ‡
102	July 23, 1952	Blood	14/5/53 24/8/53 28/7/54 2/2/55	Blood Blood Sporozoites Blood	† ‡ ‡ ‡ †

* Shortened infection † Transitory infection ‡ No infection visible

It will be noted that when blood containing *P. cynomolgi* is inoculated into monkeys immune to this species, usually no visible ... follows, if parasites appear, they are very scanty and persist for a ... Sporozoite infections are no more effective.

*Strain originally came from the ... of Ind ... the Rockefeller Foundation, New York

RESULTS OF INOCULATING *PLASMODIUM GONDERI** INTO MONKEYS IMMUNIZED AGAINST *PLASMODIUM CYNOMOLGI*

Fifteen mls of blood were withdrawn from a rhesus monkey which had a chronic infection of *P gonderi* The blood was citrated and was divided into five equal portions, each containing about 250 000 parasites These were inoculated into four immune monkeys (Table I) and into one control (M 152) The course of the ensuing infections was studied in daily blood films, and the density of parasitæmia is shown in Table II Unfortunately, the control monkey died after 11 days, but the normal course of this infection in *M mulatta* is sufficiently well known for us to be able to predict what would have happened in the control monkey had it lived, that is to say—a chronic infection would have developed and persisted for years

TABLE II

Course of parasitæmia of P gonderi *in* cynomolgi *immune monkeys*
Number of parasites per 10,000 erythrocytes

Days after infection	Monkey number				
	Control 152	81	99	101	102
1	−ve	ve	−ve	−ve	−ve
2	+ve	+ve	−ve	−ve	−ve
3	+ve	+ve	+ve	+ve	−ve
4	+ve	+ve	+ve	+ve	−ve
5	6	1	1	−ve	−ve
6	8	6	+ve	−ve	−ve
7	18	7	8	+ve	+ve
8	45	43	15	1	+ve
9	116	87	37	2	1
10	274	327	100	8	4
11	Died	444	71	24	10
12		121	73	68	29
13		41	31	56	124
14		19	12	34	146
15		20	12	12	182
16		16	13	9	105
17		36	11	18	35
18		43	7	21	5
19		77	2	25	1
20					
21		60	4	23	8
22		47	3	9	8
23		33	2	6	13
24		14	1	6	35
25		16	3	15	28
26		17	1	25	52
27					
28		14	+ve	31	24
29		11	+ve	23	34
30		17	+ve	36	23
31		51	+ve	11	38

*Strain obtained from the School of Tropical Medicine, Antwerp

cross immunity between two organisms must mean the possession of a common antigen, its absence the lack of one indicating a fundamental difference which may be specific in character. The absence of cross immunity alone would have little diagnostic value, but when associated with other evidence might provide useful confirmation of the status of a parasite. Our experiments suggest that there is no cross immunity between *P. cynomolgi* and *P. gonderi* in rhesus monkeys, confirming that they are two distinct species. Table III presents the characters which may be used to differentiate these two species.

TABLE III

Differential characters of Plasmodium cynomolgi *and* Plasmodium gonderi

Character	*P. cynomolgi*	*P. gonderi*
Origin	East Indies	West Africa
Host (Vertebrate: nature)	*Macaca irus*	*Cercocebus* spp.
Host (Insect: laboratory)	*A. maculipennis*—excellent	*A. maculipennis* poor
Course of infection in rhesus	Self-limiting	High chronic parasitaemia
Time of rupture of schizonts	Early morning	Late afternoon
Cross immunity	Nil	Nil
Effect on erythrocyte	Distinct enlargement	Slight enlargement
Double chromatin dots	10 per cent in young rings	Rare or absent
Number of merozoites	15.4	12

Both species have a 48 hour blood cycle, produce Schüffner's dots, show double invasion of red blood cells, exhibit indistinguishable gametocytes and have sporozoites of equal length (11.5 μ dried).

SUMMARY

1. Monkeys immunized against *P. cynomolgi* are susceptible to *P. gonderi*.

2. A monkey cured of a long standing infection of *P. gonderi* proved to be susceptible to *P. cynomolgi*.

3. This absence of cross immunity plus other evidence indicates that the two species are distinct from each other, though both belong to the 'benign tertian malaria' group.

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A NEW APPROACH TO THE EPIDEMIOLOGY OF MALARIA

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(September 5 19 5)

OUR knowledge of the epidemiology of malaria owes more to workers in India than in any other country of the world It was first advanced by Dempster (1848) who established the general circumstances in which malaria occurred, the means by which it could be accurately measured and some of the means by which it could be prevented The transmission of the disease by mosquitoes, the differing vectorial capacity of anopheline species the causation and nature of epidemics and the nature of hyperendemic malaria were all described in India as the highlights of a mass of work which has no comparison elsewhere Before 1929 this was distributed in a number of journals but since then has been for the most part collected in one series which is worthy of the work which it records

The author owes much to the example of workers on malaria in India, to the experience he has had there ar
in India with that elsewhere The
understanding Types of malaria
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1950*a* *b*, 1952*a* *b* 1953 1955) which though essentially simple in themselves are partly written in a language unfamiliar to most malariologists, of mathematics The object of the present paper is to translate much of this working attempting to expose the methods of work used and show how the products of mathematical analysis can be used to elaborate understanding of the normal epidemiology of malaria in the field

FACTORS INVOLVED

The state of parasitæmia is an intermittent one varying in length with characteristics of the parasite and the immunity of the individual concerned Proper account can be taken of these variations but it is convenient to consider happenings in a totally non immune person in whom it has been shown that *Plasmodium falciparum* infection may typically be patent on about 200 to 250 days whilst gametocytes may be present on about 80 days following a single infection On each of these days the patient may be bitten by vector mosquitoes let us say in illustration by about 10 and if the infection is established it proceeds through oocyst development to the production of sporozoites The time taken for the production of sporozoites is a function of temperature Figure 1 shows the approximate speeds of development of *P falciparum* and *P vivax* in the mosquito to the stage of production of sporozoites In ordinary tropical climates one might say that the normal time of development of *P falciparum* is 12 days, though this may be much prolonged in cooler weather The proportion of mosquitoes which survive sufficiently long for this development depends on the mortality to which they are exposed Figure 2 shows how this varies with mortality Circumstances in which the daily mortality is ten per cent—a not unreasonable figure—may be used in illustration, in which case about 30 per cent will survive for this period

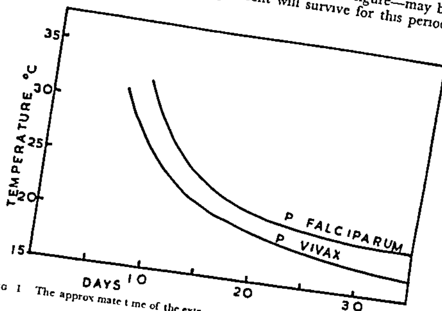


Fig 1 The approximate time of the extrinsic cycle in relation to temperature

Next comes the question of how long the mosquito may be expected to survive to bite other people should it have lived long enough for the development of sporozoites Again it depends on the mortality to which the mosquitoes are exposed and is illustrated in Figure 3 In the example chosen with a 10 per cent mortality the expectation of such life would be about ten days The number of

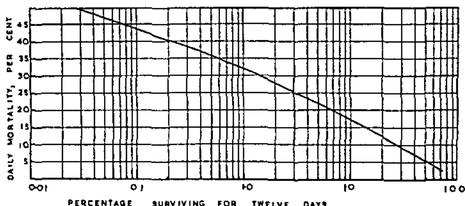


Fig 2 The effect of mosquito mortality on survival through the extrinsic cycle

people whom the mosquito will bite during that period depends on its biting habit, under tropical conditions the majority of anophelines take a blood meal once in every two days but their habit of selection of man or other animal varies very greatly In some, for instance *A gambiæ*, the meal is almost invariably on man, in others, the meal is rarely on man if other foods are available In the example used for illustration it may be taken that it feeds normally on man and once in every two days, ds after the development ı which it thus transfers of the individual, but period which can be taken as ten days, and in the case of *falciparum* infections by a further ten days before gametocytes appear and the case becomes infective to mosquitoes

CONCEPTS

In the example chosen the individual was bitten on each of 80 nights by ten mosquitoes of which 30 per cent survived for the development of sporozoites, and each of which took five subsequent feeds There is a potential infection of as many as 1,200 people from the original This introduces the idea of a reproduction rate, the number of secondary cases which potentially could be infected

eventually restrain it In the case of insect borne diseases there are two brakes, one is the existence of previous infections in the individuals who receive infective bites, so that the subsequent bites are non effective and do not actually produce new cases of the disease The other brake is the occurrence of superinfection in the mosquito, which may have a previous infection so that a second infection does

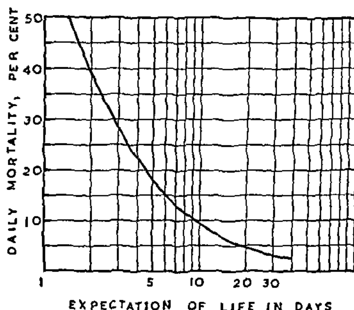


Fig 3 The effect of mortality on expectation of life

not materially increase its infectivity These factors together reduce the gross reproduction rate to a net one which may be much lower Should this fall below one, successive generations of cases will be smaller than their predecessors and the disease will disappear, should it be greater than one, successive generations will increase and the disease will mount in the population Obviously the objective of all control is to keep the reproduction rate below one so that successive generations decrease in size and the disease disappears Since in the last resort when it is in process of disappearing, the gross and net reproduction rates are the same it can be said from the start that the objective is to reduce the gross reproduction rate below one

The idea of a critical level is also introduced here It is not necessary to eliminate transmission completely in order to get disappearance of the disease but *only to reduce it below some significant level*, after which the disease will decrease indefinitely This is a most important concept in general epidemiology and particularly in that of malaria, and explains the occurrence in some parts of the world of anophelism without malaria, the transmission being at such a low rate that the disease automatically extinguishes itself

INTERACTION OF FACTORS

Fundamental epidemiology considers this cycle of transmission in various stages The sporozoite rate depends on the number of gametocyte carriers in the population, on the period of the extrinsic cycle and on the mortality rate of the mosquitoes in a manner illustrated in Figure 4 The mortality is here put as a survival

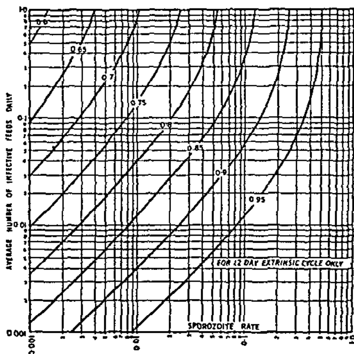


Fig 4 —A series of graphs showing the sporozoite rate corresponding to given frequencies of infective feeds Each graph refers to a different *probability of survival which is shown on the line The frequency of* infective feeds is the product of the frequency of biting man and the infective gametocyte rate

rate, 0 95 meaning that 95 per cent survive through one day The graphs have [illegible] per cent chance of a mosquito biting an actually infective person on any particular day, for in these conditions in Africa the *prevalence of infective* people is reduced by the occurrence of immunity In parts of India where malaria is transmitted by *A culicifacies* very much lower *sporozoite* rates of the order of 0 1 per cent are often recorded In an extensive series of surveys made by Russell and his co-workers in Madras it was 0 064 *per cent; this* was attributable to a 22 5 per cent daily mortality of the mosquito which took only, on the average, 1 out of 40 of its feeds on man, an extrinsic cycle for *P. vivax* of about nine days, and a gametocyte rate in the population of about 13 per cent.

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each case the curve mounts to a plateau Where the inoculation rate is lower than the recovery rate this plateau is below the level of 100 per cent infections In other cases the parasite rate rises rapidly to 100 per cent and subsequently remains at that level, the majority of individuals actually suffering from two or more concurrent infections This theoretical graph can be and has been checked against similar curves observed among infants in nature The curves fit with extraordinary accuracy in a large number of cases, which establishes the general veracity of their shape and derivation There are however, a number of cases in hyperendemic parts of Africa where the inoculation rate derived from this form of working is very much less than that derived by entomologists examining the numbers of mosquitoes and their sporozoite rates, and it is thought that the explanation lies largely in the very low grade infections of the mosquito, consequent on low gametocyte counts in the population which is highly immunized

Fig 5 —Theoretical infection rates by ages corresponding to various inoculation rates (*h*) The limiting value for all values of *h* exceeding 0 005 is 1·0

In nature the parasite and sporozoite rates are dependent on each other An increase in the parasite rate automatically increases the sporozoite rate, which in turn increases the parasite rate, and so on *ad infinitum* until the brakes on multiplication the occurrence of superinfection in man and the mosquito, bring increase to an end The next process in analysis is to examine the form of happenings when both the parasite rate and the sporozoite rate are allowed to vary in a manner dependent upon each other Assuming for the sake of illustration that there has been some mild malaria in a community and thus a reservoir from which the disease can arise, and that transmission is abruptly increased, analysis produces the form of epidemic curve which would result It has a curious form

starting with an original abrupt step, followed by a pause, and after a lag by a second more rounded curve.

Epidemics in nature are almost always mixed ones of *P. vivax* and *P. falciparum*, ... of *P. vivax* alters the timing ... together form a combined ... compared with actual ... lon epidemics of 1934/35,

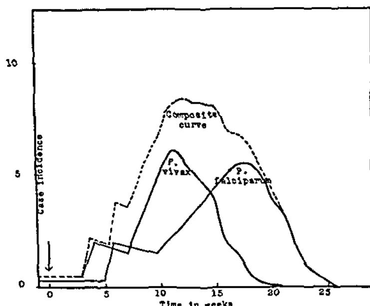


Fig. 6 Two synthetic epidemic curves built on identical data except for differences in incubation interval and extrinsic development, corresponding to those of *P. vivax* and *P. falciparum*

and in most subsequent ones, one can trace the same general form. All natural epidemics do in fact consist of two separate curves as has been shown, and the occurrence of a very abrupt start, the preliminary appearance of *P. vivax* and the ... ted features. ... s of Ceylon ... multiplication of mosquitoes necessary to produce such a catastrophe.

Epidemic curves reflect the admission of new cases but there are two factors new cases and the parasite rate The latter mounts from the start of the epidemic to achieve a plateau, which may be 100 per cent of the population or less In analysis it is represented by a theoretical formula which cannot be directly checked in nature, because when this steady stage is reached immunity sets in, alters the value of one of the factors involved—the duration of the disease—and invalidates

direct comparison The expression might, therefore, remain one of theoretical academic interest except that it can be used in subsequent examination of the stability of equilibrium, a very important concept which may be illustrated by a mechanical analogy no engine however well governed runs perpetually at the same speed, some increase of the load on it produces some slight decrease in speed though this may later be adjusted by the governing mechanism Now imagine two engines one of which is fitted with a reasonably efficient governor which maintains it running at roughly the same speed whatever the load that may be put upon it, and another which has an extremely inefficient governor so that with variation of

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overlap of infections in the mosquito and the more efficient the governing mechanism, resulting in a much more stable epidemiological condition with less tendency to vary from the mean It is in exactly this characteristic of degree of

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several years However, in other places and notably in northern India, parts of Pakistan and in Ceylon, the variations from year to year are extreme In some there is a periodic variation with a cycle of about eight years, but apart from this good and bad years follow each other in an irregular manner Examination of the vectors of malaria shows that these two types do in fact depend on the longevity and the biting habit of the mosquito as theory had indicated they would

EPIDEMIOLOGICAL TYPES

By this route the concept of two quite different types of malaria, stable and unstable, is introduced The first is caused by transmission by a mosquito which feeds often on man and has good prospects of life The critical level is extremely low and in consequence anophelism without malaria is extremely rare The disease shows little tendency to fluctuate from its normal, and epidemics amongst the indigenous inhabitants are rare In consequence of the regular transmission of the disease immunity is fairly readily established amongst the local population, adults often show a firm resistance to it, and the disease is very difficult to control by anti larval measures and relatively difficult by imagicidal measures On the

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greatly from year to year, sometimes with dramatic epidemics of extreme severity

as those in Ceylon and the Punjab The irregularity of transmission and the occurrence of consecutive years when it happens only on a small scale, results in a poor stimulus to the develpment of a firm immunity in a population

These processes can show what is happening in epidemiology and why it is happening, why malaria is so vastly different in, for instance, central Africa where it is of the extreme stable type, and in Ceylon and the plains of India where it is of the extremely unstable type, one can in fact map out in the world zones where the epidemiological types differ In northern Europe, for instance, malaria was relatively unstable, and is in fact in process of natural control by deviation of anophelines from man, whereas in southern Europe it is of the extremely stable type and remained unchanged until the development of imagicidal control in recent years

CONTROL

The object of all control is to reduce the reproduction râte below one Without suggesting that the rate should be accurately calculated in every region, one should at least form a concept of the nature of the reproduction rates and the degree of reduction necessary to establish control of the disease Theoretical examination can show the changes in the density of anophelines, in their daily

and longevity of the local vector, from them to determine the actual amount of transmission and the potential amount should the entire population be non-immune, in the form of the basic reproduction rate, from these, estimates must be made of the changes in conditions necessary for control It is then for the executive to determine how these changes can best be produced, though in most cases it will be by the use of residual insecticides The determination of the actual mortality achieved by the use of particular insecticides in the field, using experimental trap huts, when related to estimates of the mortality necessary can, undoubtedly, avoid wastage

Though the immediate attack should usually be through insecticides, their

"spontaneous' regressions have occurred in places where the local mosquito is readily deviated from man to cattle, and it seems probable that the regression follows some slight change in agricultural pattern which has led to the more ready availability of animal food There are large areas in India where even before the application of the modern methods of control, malaria was absent despite the presence of some vector mosquitoes, and there are other considerable areas where the disease has shown itself to be evanescent, coming and going in an irregular way following minor changes in the environment This indicates that over very large tracts indeed the basic reproduction rate was naturally near its critical level

of one, and the amount of change needed to bring it permanently below that level would be small Any deviation of the mosquito from man to animal must act in this direction and the influence of such deviation is very marked The most interesting epidemiological study in India therefore lies in those areas of anophelism without malaria, and should concern itself with the precise reasons why malaria is absent, and the levels of mosquito prevalence, longevity and anthropophilism which permit the co existence of man and mosquito without the transmission of the disease With the knowledge gained in such studies the present great malaria control programme could rationally go on to one of elimination throughout [illegible] would [illegible] uction [illegible] e and northern America is an insurance in those areas

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SOME PROBLEMS ON CHEMOTHERAPY OF MALARIA.

BY

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(September 10 1955)

WITH the advent of modern synthetic antimalarials, treatment of acute attacks of malaria nowadays presents few difficulties The most powerful of the series (by oral route), as judged by the speed of action in relieving clinical symptoms as well as by the clearance of asexual parasites from the peripheral circulation, are the drugs of 4-aminoquinoline series Even in extremely severe cases, parenteral administration of chloroquine preparations has been found to be as effective as quinine though some consider that the former is somewhat better. However, that would need detailed comparative studies against all the available strains of plasmodia before a final conclusion can be drawn

As a blood schizonticide, neither proguanil nor pyrimethamine is as rapidly active as the 4-aminoquinolines Besides their comparatively slower action,

Although satisfactory reports on mepacrine have been presented by many workers, ... that compared to the ... and that it is likely to ... though in a very small percentage of cases In repeated doses quinine acts almost as fast as mepacrine

Thus the choice of antimalarials for treatment of acute attacks of malaria naturally falls on the 4-aminoquinolines administered orally as a single dose of 0·6 gm (adult) in partially immune population, if the condition is not too serious Under emergency conditions and in cases where the patient is unconscious or if there is incessant nausea and vomiting, parenteral administration of chloroquine or quinine hydrochloride or dihydrochloride would obviously be called for.

Thus in the discovery of compounds like the 4-aminoquinolines a stage has now reached that perhaps further development of a more potent and rapidly effective remedy for clinical cure may not be necessary in view of rapid reduction of the incidence of malaria on account of large scale control measures

Prima facie it would appear that the main problem in the treatment of malaria has practically been solved But on deeper consideration, it becomes evident that there are still many lacunæ in our knowledge of the subject For example, it is not clear why certain drugs like quinine, mepacrine and the 4 aminoquinolines which are such powerful blood schizonticides, yet have no effect on the sporozoites or the tissue forms (primary or secondary) of the plasmodia Again drugs of the 8 aminoquinolines which are tissue schizonticides, particularly effective against the secondary exoerythrocytic forms, have poor action against the asexual erythrocytic forms, specially in respect of *P falciparum* Similarly, exp
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plasmodia Further, it is also common experience that some strain of a plasmodium is highly susceptible to a particular drug while others are comparatively refractory and need much larger doses It is also not clearly known as to why should plasmodia develop resistance to certain particular groups of compounds like proguanil or pyrimethamine, and not against drugs like quinine, mepacrine or the 4 aminoquinolines

Factors like the phases of plasmodium life cycle, somewhat different pattern in the life cycle of *P vivax* and *P malariæ* as against *P falciparum* in the human host, the metabolic processes of plasmodia in the tissues like the liver and also in the blood, the chemical constitution of antimalarials and their effect on plasmodium metabolism, metabolites of antimalarials, pharmacological considerations like break down products, absorption and distribution of the drug in the tissues of the host thereby aiding its penetration, and many other problems of similar nature have to be carefully considered

As to the life cycle of malaria parasites, most of the lacunæ in our knowledge have been filled since the discovery of the tissue phase Although, it is the general opinion that secondary exo erythrocytic forms develop in *P vivax* and *P malariæ*, there is reason to believe that such forms are absent in *P falciparum* As to why such stages are not developed in the
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Further, it is well known that cert
methamine and the 8 aminoquinolines are effective against the primary tissue phase of this plasmodium but not against the others Since the rate of absorption, distribution, and tissue concentration of the same drug could not be fundamentally different in the same host, it is difficult to understand as to why there should be such a marked difference in the reaction of plasmodia to these compounds Naturally, therefore, this leads one to speculate that perhaps the metabolic processes of the pre erythrocytic forms of *P falciparum* are different from those in respect of *P vivax* and *P malariæ* Again it would appear that perhaps similar differences exist in the metabolic processes in the same plasmodium, like *P vivax* at the primary and secondary exoerythrocytic forms, because 8 aminoquinolines, though active

to be an extension of the sporogony phase of the plasmodium yet drugs which are effective against the tissue phase are totally ineffective against the sporozoites in spite of the somewhat similar cytological character Since it is believed that antimalarials act by interfering with the enzyme system there is reason to believe that the metabolism of the two stages sporozoites and pre erythrocytic forms are different This variation perhaps depends on the particular environment where they are usually lodged like the salivary glands or the liver

There is also the possibility of differences in the metabolic processes of tissue forms and erythrocytic forms firstly because powerful blood schizonticidal drugs like quinine 4 aminoquinolines etc are ineffective against the tissue forms of the same plasmodium and secondly powerful tissue schizonticidal drugs like 8 aminoquinolines are poor blood schizonticides Again it may be noted that most of the existing antimalarials which are powerful blood schizonticides are poor gametocytocidal drugs On the other hand 8 aminoquinolines which have powerful gametocytocidal action (also tissue schizonticides) are poor blood schizonticides Could there be differences in the metabolic processes even in the sexual and asexual forms of the same plasmodium? Also could the metabolic pattern of gametocides and tissue forms of the same plasmodium have some degree of similarity?

As to the metabolic processes of malaria parasites and drug action the present day knowledge is limited Although quinine has been known for centuries to have specific action against malaria parasite it is surprising to note that as yet so little is known as to how it acts This is true for other antimalarials as well The earliest workers like Christophers and Fulton (1938) demonstrated that quinine, mepacrine and pamaquin inhibit the oxygen consumption by the parasites Mepacrine has been shown to interfere with the respiration of malaria parasites but quinine much less so Silverman *et al* (1944) believe that quinine affects the

[illegible] erythrocytic forms of *P gallinaceum* in tissue culture (Tonkin, 1946) According to Hellerman *et al* (1946) atabrin and quinoline bases are enzyme inhibitors These are likely to combine with certain acidic groups of the enzymes If such groups combine with co-enzymes a competition is set up between co-enzyme and the inhibitor Work and Work (1948) believe that this inhibition may not be specific to one enzyme or class of enzymes According to them the danger of misinterpreting the action of an inhibitor as a result of testing on an insufficient number of enzymes is well illustrated in the case of the antimalarial drugs' Findlay (1951) observes that quinine mepacrine and pamaquin might interfere with a number of reactions essential for the metabolism of malaria parasites

According to him, "there is still uncertainty as to how far any such inhibition is responsible for antimalarial action" In the same way, there is hardly any indication as to the mode of action of proguanil

As to the correlation between chemical constitution and antimalarial drug Magidson *et al* (as quoted by Findlay, 1951) suggested that different parts of the molecule of a drug, like mepacrine, have different functions and that basic side chain is primarily of pharmacological importance, controlling absorption and distribution of the drug in the host and aiding its penetration into the parasite, while the substituted acridine or quinoline nucleus is responsible for the plasmodicidal action But by experience, and from studies on newer antimalarial drugs, it has been observed that it is difficult to establish such correlation Findlay (1951) observes that "to attempt to correlate chemical constitution and antimalarial action has so far proved an impossible task"

It is also not clearly understood whether a compound exerts its act through the parent or its metabolites It is known that quinine is degraded the system to a 2-hydroxy derivatives But this has been found to be inferior quinine (Marshall and Rogers, 1948) Spectrographic study of mepacrine do not indicate acridines as the possible metabolic products During their studies o pamaquin, Josephson, Taylor *et al* (1951) had observed that concentrates obtaine from blood, tissues and droppings of the chickens treated with pamaquin, possesse antimalarial activity *in vitro* equivalent to 16 times that of the parent compound This activity could not be accounted for on the basis of pamaquin present in these concentrates But subsequent *in vivo* studies on one of the metabolites isolated by (Josephson, Greenbergh *et al*, 1951) did not show any antimalarial activity (Schmidt, 1951) Elderfield and Smith (1953) were also unable to establish any definite metabolite of pentaquin Similarly ultraviolet irradiation of 4-amino-7-chloroquine derivatives and study of their breakdown products, did not reveal any new product (Price *et al*, 1948)

Hawking and Perry (1948) suggested that proguanil itself is not active it is converted to an active metabolite Carrington *et al* (1951) and Crowt and Levi (1953) were able to isolate an active metabolite of proguanil as well an inactive compound originally isolated by Crounse (1951) The active metabol is a dihydro triziane derivative but according to Schmidt *et al* (1952), the pare compound was found to be two to four times more active than the metabolite Subsequently, however, a large number of triazine compounds have bee synthesized and some of them have shown high degree of activity against *P gallinaceum* in chicks

In view of the points raised above it is apparent that the existing knowledge on the problem of chemotherapy in malaria is still limited At the moment our primary objective is to develop a suitable compound which in non-toxic doses is highly and equally effective against all the phases of the plasmodial life cycle, or at least against the asexual erythrocytic and tissue forms In other words, it should be a powerful blood schizonticide as well as tissue schizonticide If this proves effective against the gametocytes and sporozoites as well, it would be an add advantage This is particularly necessary in case of *P vivax* infection for thoug it is quite easy to effect a clinical cure with the usual antimalarials, its radical cure continues to be a baffling problem No doubt some of the newer 8-aminoquinolines

possess curative action but there are always the toxic hazards encountered, though in small number of cases.

In order to achieve this objective, it would be essential to understand clearly the metabolic processes of plasmodia at all the phases, particularly the tissue and blood forms. Once the basic requirements of the plasmodia are well understood, [illegible]

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ANOPHELES RESISTANCE IN RELATION TO MALARIA CONTROL PROGRAMME PLANNING

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(July 27 1955)

INTRODUCTION

THE great expansion in malaria control activities which has taken place within the past ten years with the development of D D T and related residual insecticides has created many new problems and increased the importance of many old ones In addition to perplexing problems related to the development of effective and adequate malaria control organizations, is the problem of resistance to residual insecticides by anopheline vectors

The extent to which these issues can be resolved naturally varies with the existing situation in each country, including financial resources, the availability of suitably trained professional personnel, ways of thinking, and competing exigencies In this connection, the author is reminded of his experience of 25 years ago in a State-wide programme of malaria control in one of the States of the United States of America, in which the situation can be summed up by the following bare facts Area served—58,000 square miles Population served—three million Number of malaria cases—50,000 to 100,000 Number of professional personnel assigned to malaria control—one Paradoxically, it was not until malaria had largely ceased to be an important socio-economic burden that funds became available for the development of adequate malaria control organizations in this and other malarious States of the United States

Under such circumstances it was futile to propose new plans for the existing malaria control "organization" to carry out, which invariably required additional trained personnel Today, throughout the world, malaria control programmes fortunately are staffed somewhat more adequately, but major shortages of key personnel are still all too common Such shortages understandably impede the adoption of "ideal" plans based on theoretical concepts, some of which may be involved in this article

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ANOPHELES RESISTANCE

In considering any matter of insect resistance, two governing natural laws should be recalled to mind One is that the development of resistance is a product of selection pressure, its duration, and the genetic capacity of the species to develop resistance The other is that, barring eradication, any species inevitably will develop resistance of one type or another, provided the degree and duration of selection pressure in combination are sufficient to threaten species survival

When one surveys the results of ten years of global application of the chlorinated residual insecticides for agricultural, public health, and pest control purposes the comparative lack of confirmed resistance development in the field among the anophelines is little short of amazing This is especially true of many of the more anthropophilic anopheline species which, in some areas, have been bombarded for eight years or longer in specific localities with D D T residual house spray Malaria has been eradicated in extensive subnational areas where the biotic potential of the disease was high, with and without vector eradication, and has been controlled in other far more extensive areas of high biotic potential Malaria eradication also has been realized in other extensive areas where the disease was not so firmly intrenched In a few special cases where the vector had not achieved a status of long, indigenous adaptation, species eradication was even achieved as a partly unexpected dividend from malaria control operations Yet, so far, only four of about 50 significant anopheline vector species are considered to have acquired physiologic resistance in local or more extensive areas These are *Anopheles sundaicus* in Indonesia, *A maculipennis*, *A sacharovi* and *A superpictus* in Greece, and *A sacharovi* again in Lebanon (Pampana, 1954, Garrett-Jones, 1954; and Crandall, 1954 1955) With the exception of Lebanon, physiologic resistance development has occurred in the presence of adulticidal treatments *cum* larviciding *although these selection pressures were not necessarily applied continuously and* concurrently Even in Lebanon, the possibility of larval exposure incidental to agricultural insecticiding cannot be ruled out Earlier reports of resistance in *Anopheles quadrimaculatus* in the T V A area of the United States of America have not been substantiated (Hawkins and Hall, 1954) The species is under larvicidal treatment in this area, but such treatment is restricted to federally-owned properties bordered by private lands

Behaviouristic resistance as a developmental factor cannot be as readily evaluated nor, as pointed out by others, is it necessarily adverse to man's interest [illegible] both to anophelines which do not normally enter or [illegible] those possessing hyper-irritability [illegible] t is at times difficult to determine whether observed behaviouristic resistance was a pre-existing characteristic of the dominant population group, *of an important biotype fraction which has not* increased in prevalence, or whether the resistant biotype has become more prevalent as a result of the selection process An example of behaviouristic resistance which has impeded malaria control is provided by *A sergenti* and *A superpictus* in the Jordan Valley (Farid, 1954) One which has not prevented malaria control is that of *A albimanus* in Panama (Trapido, 1952 1954).

Compared with the house fly, this relatively favourable state of affairs reflects the lower genetic capacity of the genus *Anopheles* to develop resistance, supplemented in some cases by fewer generations per year The exposure of a smaller fraction of the species population to insecticides is an added possibility. The latter factor highlights the well established principle that residual house spray in malaria control is a highly selective tool which is intended to intercept only that fraction of the species population which is infective to man

Yet, the importance of anopheline resistance should not be minimized It is already a problem of major importance in some of the countries or local areas in

spread of anopheline resistance, rather than contending with existing resistance problems

Efforts which are being made, or might be made, to solve the resistance problem may be divided into two categories (1) Laboratory studies, and (2) Field operations

LABORATORY STUDIES

These consist of (1) Basic physiologic, biochemical, and genetic studies on the mechanism of resistance in arthropods, particularly anophelines, and the genetic processes by which physiologic and behaviouristic resistances are developed, and (2) the development of new insecticides, formulations and techniques of application The apparent purpose of the basic studies is to permit making more intelligent searches for new insecticides and synergists, but the theoretical implications of such research extend further

In combination the present main hopes of such studies are in the following directions with the proviso that any insecticide which satisfies one or more of these objectives must also be relatively safe to man in application and in use, and must be economical in cost

A Development of an even more effective residual insecticide which will

test results of 70 to 90 per cent tends to be exophilic in resting place with respect to human dwelling places, while the multidentate zoophilic race tends to be endophilic This hypothesis, accordingly, may not apply in exceptional cases

B The development of new insecticides with differing periods of residual effectiveness, but which in other respects would have substantially equal merits

By selecting for each area an insecticide having an effective residual life equal to but no greater than, the length of the seasonal period of disease transmission selection pressure during the remainder of the year could be avoided Such insecticides should have high effectiveness with an abrupt termination point Tl merits of this objective are sharply limited by the facts that (1) a high proportio of the number of annual generations of vectorial species in the more malarious area occurs within the malaria transmission season, (2) variation in length of effective life can be achieved with existing insecticides to a considerable extent by choosing between available insecticides and by selection of dosage rate, and (3) it is not operationally feasible for residual spray crews to apply insecticide to all houses at the optimum moment—several months may be required for a spray crew to cover its territory with a single application

C The discovery and development of new insecticides formulations, and techniques of application by both haphazard and systematic methods The development of very high resistances and cross resistances to many of the newer insecticides by arthropods of agricultural or public health importance has generated what appears to be a perpetual race between man and insect in insecticide development Although centered mainly on agricultural insect problems, the control of the house fly and various culicine mosquito species also provides important motivation in the quest for new insecticides In a mosquito abatement district in the State of California in the United States, for example, the entire list of chlorinated hydrocarbon insecticides was thrown into the discard three years ago due to mounting resistance by *Culex tarsalis* and *Ædes nigromaculis* (Geib, 1955) Since then, a number of organic phosphorus compounds have been resorted to this larviciding programme

Such further new developmental work possesses somewhat less direct sig ficance in malaria control, in view of the slow rate of resistance development i anophelines to residual adulticidal treatments the apparent absence of tot spectrum cross resistance in them, and the present availability of one or mor acceptable alternative residual insecticides in the chlorinated hydrocarbon group But there is always the possibility that a new insecticide may evolve which is more effective or more economical, and yet safe for extensive indoor application

FIELD OPERATIONS

The foregoing laboratory studies have significant potential value in malaria control and eradication, and should be pursued But it is of great importance tl the management of malaria control operations in the interest of avoiding resistan not be neglected in any particular In a large scale programme even min operational changes may be difficult or slow to execute, and may temporaril impede operational efficiency and the accomplishment of other urgent objectives Programme decentralization, although desirable in many respects, may complicate the acceptance and adoption of such changes The achievement of effective malaria control under adverse operational conditions often is an exacting and difficult task at best In spite of such obstacles, consideration of the resistance problem in programme planning and execution is essential

Differences undoubtedly exist in the genetic capacities of different *Anopheles* species to develop resistance, *and in the actual resistance of different species*, biotypes and even individuals However, the main variables within this genus in the selection pressure—duration—genetic capacity—equation are considered to be selection pressure and its duration Certainly this is the case when the house fly is used as a plane of reference Were it not so early, extremely high resistance would have appeared many years ago in those of the more anthropophilic species which also had genetic potentialities materially higher than the mean level for the genus

While the degree of selection pressure exerted is very importantly affected by behaviour of the adult anopheline, it is otherwise a controllable variable *Duration of pressure is totally controllable aside from the inherent characteristics* of the insecticide employed Even these characteristics can be modified by varying application rates and practices

The *present main trend of thought in certain* malariological circles is to achieve the eradication of malaria as rapidly as possible, and in as large areas as possible, in order to permit the interruption or termination of residual house spraying Avoidance of resistance is only one element in the total motivation and justification for this concept, but it is a carefully considered factor

It may be postulated that the optimal condition favouring *Anopheles* resistance development which would be encountered in the field is that of moderately high selection pressure applied perpetually The degree of pressure would be as high as possible without eradicating the biotype, species, or parasite In theory, departure in either direction from this optimal selection pressure should reduce the rate of resistance development or totally avoid it

It is generally considered that even very low selection pressures continued long enough will result in som [illegible] doubt this is true of isolated populations, [illegible] he case of many of the more zoophilic [illegible] unexposed populations *Anopheles albiman* [illegible] houses at dusk or after dark, dispersing within the night or at dawn to concealed outdoor daytime *resting places Precipitin tests for human blood in this species are* commonly below five per cent Assuming the figure of five per cent to roughly represent the percentage of the population which becomes exposed to D D T. residual spray within houses in obtaining a single blood meal, that the percentage of survivors from this exposure is not over 20 per cent (or one per cent of the total population), and that this one per cent is then diluted 95 fold by zoophilic feeders in the perpetuation of the local species population, it is apparent that the degree of selection pressure would be negligible While this example is deliberately oversimplified, it illustrates the principle of population dilution in combination with low selection pressure on the local species population

However, avoidance of *Anopheles* resistance is not an end unto itself, nor is it an overruling consideration in most areas at the present time For this reason, overall objectives are best served by increasing the intensity of selection pressure as a calculated risk in order to achieve more rapid malaria eradication and to terminate residual spraying

Malaria control and malaria eradication have much in common, but differ in important particulars from a programme design standpoint Both concepts demand in principle a high order of operational competency in the malaria control

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profession is basically the epidemiological observation of the disease in man and, traditionally in many areas, over all command of programme

Globally, programmes for malaria control *per se* may be considered as having conformed to two main patterns The more common programme has followed the concept of prompt, effective suppression in project areas where operations were carried on The other pattern, dictated by limitations of supplies and equipment in relation to magnitude of problem, has been aimed at controlling the greatest number of cases of malaria with available resources By use of relatively high D D T dosage rates, coupled with an optimal frequency of application, malaria transmission in the first pattern might, for example, be reduced 80 per cent in the first year In the second pattern, the same quantity of D D T might be spread over twice as many houses with the expectation of reducing malaria transmission by only 60 per cent, but among twice as many people Although the objective of the second pattern is praiseworthy, and was no doubt fully justified a number of years before the threat of resistance became apparent, careful re examination is warranted if such programmes still exist

As with species eradication, malaria eradication is directly dependent upon eliminating the last surviving reproduction source, in this case the gametocyte carrier, from each useful unit ' area This is the major point of difference between malaria control and malaria eradication In consequence, malaria eradication, in principle demands a higher order of programme effectiveness, as previously mentioned It also demands the regrouping and extension of project areas along different lines than with malaria control programmes Generally, malaria control and malaria eradication operations should be initiated in areas

malaria control, this would be in conformance
greastest number of cases at the lowest cost,
be to lower malaria rates to parity with
adjoining less malarious areas Having achieved this parity, however, the project area in a malaria eradication programme should be expanded as rapidly as possible toward inclusion of the total malarious territory comprising the trading area Since such territories generally conform to transportation routes, they are likely to be irregular in shape Expansion into areas of low endemicity within such a territory would have priority over initiating work in a new, more malarious, but remote area

The absolute prevention of reintroduction of malaria into a clean area is, of course not to be expected until national, regional, or even hemispheric and global eradication has been achieved in all areas from which travellers may originate The goal is rather to reduce the frequency of reintroduction to such a low level that the prospects of restoring large scale malaria transmission and the burden of malaria surveillance are minimized

In the interest of reducing the hazard of resistance development, as well as economy of effort, many short cuts in finally terminating residual spraying in an area may be postulated Certainly, continuation of full scale spraying in a district of say, a million people, until several years after the termination of

adequacy of malariologic services There is almost certain to be an acute shortage in the quantity of such service which might ideally be desired in every country where malaria is a primary public health problem Thus, rather than creating a problem of technological unemployment among malariologists, D D T potentially has created a far greater need than ever before existed

should antedate residual house spraying

The first measure is the determination of prevailing resistance baselines for each vector species at judiciously selected observation posts and recurrent testing of the resistance level At least two published objective tests have been developed for this purpose (Expert Committee on Malaria World Health Organization 1954 and Fay *et al*, 1953) Such testing is underway but should be far more extensive When resistance is detected on operating projects by less sensitive methods, it is often too late Diagnosis is never a substitute for cure, but is an essential prerequisite

The second measure is the careful restriction of use of chlorinated hydrocarbon insecticides for anopheline larviciding The circumstances under which the World Health Organization Expert Committee on Malaria has indicated such larviciding should be practised, do not preclude the development of resistance, but do tend to limit its occurrence to restricted geographical areas

Instances in which larviciding for malaria control should be the method of choice over residual house spraying on economic grounds consist mainly of urban areas or small breeding surfaces in isolated communities such as oases Larviciding on biological grounds also has been advocated for the control of important exophilic vectors, as is repored to be the case with *A superpictus* and *A sergenti* in the Jordan Valley (Farid 1954) Justification for larviciding *cum* residual house spraying would be more often encountered in suburban areas where the joint control of anophelines and certain other mosquito species are involved, but also can be visualized in exceptional situations where malaria is primarily transmitted by an endophilic species and secondarily, by an exophilic species In the latter case, differences in breeding habitat and adult behaviour might result in the selective exposure of each species

The importance of avoiding use of the same chlorinated hydrocarbon insecticide against the immature and adult stages of the same anopheline species at the same time and place has been stressed by others Under such circumstances use of two chlorinated hydrocarbon insecticides which are not closely related has been suggested However, the extremely high resistances (up to 1300 fold) (Geib, 1955) to a variety of chlorinated hydrocarbon insecticides which have developed in the United States o ... *quinquefasciatus*, *C tarsalis*, *Aedes taeniorhynchus*, *A* ... e larvicides are intensively and extensively emplc ... the extremely high degree of selection pressure ... ol With this in mind, one might say that as long as the patient took cyanide (*i e*, larviciding) it matters little whether he also took some other relatively innocuous poison (*i e* adulticiding) at the same time It also poses the question whether the intensive use of chlorinated hydrocarbon larvicides on an extensive scale is ever warranted for malaria control, even with exophilic vectors Except where a high degree of sexual isolation exists, it may be postulated that resistance developing in a localized area will be rapidly dissipated by dilution upon interruption of selection pressure, but such development over a large area gives cause for much concern

The third measure is to pay attention to control of cause as well as control of effect Malaria eradication is one method of control of cause Another is the elimination of anopheline breeding places and prevention of the establishment of new breeding places by man The need for keeping in mind the more traditional methods of malaria control and of avoiding excessive preoccupation with the newer forms of insecticidal work has been pointed out by others (World Health Organization Expert Committee on Malaria, 1954) Yet, it is generally acknowledged that many of these measures are not susceptible of either near term adoption or of widespread adoption over the vast rural areas of the world which form the stronghold of malaria

However, in many countries, the predominance of man made over natural vector breeding places throughout large areas, is apparent This is particularly the case in India and many other tropical countries with their vast numbers of roadside borrowpits and of brick pits and their extensive irrigated acreages The elimination of existing breeding places in these categories would be a gigantic undertaking, and even the prevention of new ones is no easy matter, especially where changes in cultural practices are required

On the other hand, corrective practices in new undertakings which in themselves yield direct economic benefit (e g, water conservation in certain irrigation projects), or can be performed at nominal cost incidental to construction (*e g*, connecting shallow hillside borrowpits), are the most economical of all malaria control practices The important consideration which has been given to these problems by some malariologists in India is noteworthy

The fourth measure is further experimentation with each vector species in the field with respect to dosage rate and frequency of application of residual house sprays Early field trials of this nature were made in a number of areas in the 1940s However, they were focused on the interruption of malaria transmission as the main criterion rather than in combination with evaluating selection pressure

In countries where they are not already underway, the carrying out of further limited experimental studies in conjunction with local operating projects might well be undertaken in order to jointly evaluate malaria reduction and resistance development Would it not be desirable to deliberately attempt to induce resistance in each important vector in the smallest feasible area, in order to establish a safety factor for general programme operations or to disprove the possibility of resistance development in a particular species under the conditions of such a programme? The length of time needed to carry this through might, of course, be an important weakness

Would it not be desirable similarly to carry on other limited experimental studies in conjunction with local operating projects which would employ different dosage rates and frequencies of treatment than those conventionally used? Intensification of selection pressure on the general programme in lieu of its reduction might well be in order if the margin of safety is ample and malaria eradication could be expedited by so doing On the other hand present pressures in some

In consequence, such experiments must be standardized as much as possible and carefully evaluated No doubt, experiments along these general lines are being undertaken in some areas but are they being undertaken even to the minimum extent necessary in all indicated countries?

SUMMARY

The problem and possible solution of *Anopheles* resistance threats are considered from the standpoints of laboratory research and field operations The development of resistance is a product of selection pressure, its duration, and the genetic capacity of the species to develop resistance Any species inevitably will develop resistance of one type or another provided the degree and duration of selection pressure in combination are sufficient to threaten species survival The slowness of anophelines to develop resistance to insecticides is commented on

Three end purposes of laboratory studies concerned with *Anopheles* resistance are described Adjustment of operating practices in the field is advocated in the interest of avoiding resistance problems Principles underlying the variation of selection pressure and duration of pressure in field practices and programme design are discussed Brief mention is made of the role of certain traditional methods of malaria control and of the malaria control organization

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SPOROGONY CYCLE OF MALARIA PARASITES IN RESISTANT AND NON-RESISTANT STRAINS OF MOSQUITOES AFTER EXPOSURE TO D D T

BY

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INTRODUCTION

In a previous communication it was reported that in *A fluviatilis* and *A stephensi* (type) a sublethal contact with D D T did not inhibit the development of eggs whether the females were exposed to the insecticide before or after blood feed or as half gravids (Mohan, 1955) There was close correlation between fertilization and maturation of ovaries irrespective of the exposure to D D T Fertilized females of both the species showed a significantly higher percentage of mature ovaries than the unfertilized females It was also observed that exposure to D D T affected a fair number of gravid *A fluviatilis* and *A stephensi* in that the eggs were laid at random although suitable water for oviposition was available The present studies were undertaken to find out the effect, if any, of lethal and sublethal contact with D D T on malaria parasites in resistant and non-resistant strains of mosquitoes, respectively The effect on *P gallinaceum* of D D T orally fed to infected fowls as measured by sporozoite infection in *Ædes ægypti* was also investigated

MATERIALS

The host and parasite species used were a D D T-resistant and a non-resistant strain of *C fatigans* for *P relictum* in local sparrows, a D D T-resistant and a non resistant strain of *A fluviatilis* for human malaria and only a non resistant strain of *Ædes ægypti* for *P gallinaceum* in domestic fowls All these strains of mosquitoes were furnished by the laboratory colonies

D D T -resistant strains of *C fatigans* and *A fluviatilis* —While a fuller account of the development of the resistant strains of *C fatigans* and *A fluviatilis* will be published in due course, a few relevant details concerning each species are given below

C fatigans —Both the resistant and non resistant strains of *C fatigans* originated from the same single raft of eggs laid by a wild caught female Signs of resistance* to D D T first became apparent in the fourteenth generation as a result of the exposure of the adults males and females, to sublethal doses of D D T at each successive generation In the subsequent generations, there was some progressive increase in resistance which had reached a high level at the time of conducting the experiments with mosquitoes of the forty-third and forty fourth generations A brief resume of some of the salient points about D D T resistant *C fatigans* may be relevant at this juncture

While the non resistant strain of *C fatigans* evidenced 100 per cent mortality on being exposed to 200 mg of D D T per sq ft for one hour, the resistant strain showed little or no mortality on being subjected to similar treatment under identical conditions Adults of the latter strain were resistant not only to mortality but also to the paralysing effect of D D T The resistant strain showed *striking variations in its resistance to D D T With the dosage remaining the* same, some individuals in a given batch of females of the same generation, died after six hours of exposure, others after 12 hours, while still a few others required even more than 18 hours of exposure to die

A fluviatilis —Similar efforts were made to raise a D D T -resistant strain of *A fluviatilis* Feeble resistance† was first evidenced in the twenty-ninth generation There was slight increase in the subsequent generations but the level of resistance still remained low in mosquitoes of the forty seventh generation which were used in the experiments In this susceptible species, resistance was very late in appearance and equally very slow in building up

DEVELOPMENT OF SPOROGONY CYCLE OF *P RELICTUM* IN RESISTANT AND NON-RESISTANT STRAINS OF *C FATIGANS* AFTER EXPOSURE TO D D T

In all, four experiments were carried out Resistant *C fatigans* used in the first experiment were of the forty third generation and in the subsequent three experiments of the forty-fourth generation

Experiment 1 —Females of the resistant strain of *C fatigans* and of the non resistant strain were kept in separate cages and given an opportunity to feed on the same gametocyte carrying sparrow, the latter during the first half of the night and the former during the second half Mosquitoes of each strain which had become fully engorged were, in p... ...sed to 200 mg of D D T per sq ft for 40 minutes and the second on the third day of ...

* Indian Council of Medical Research Technical Report of the Scientific Advisory Board for the year 1952, New Delhi p 12

† Indian Council of Medical Research Technical Report of the Scientific Advisory Board for the year 1954, New Delhi p 7

the effect of these exposures was timed to coincide with the early stages of development of the parasite in the mosquito host Some blood fed females of each strain which were not exposed to D D T were kept for comparison There were thus

t and two of the non resistant strain, parison) insects They were kept in fed on ten per cent glucose solution o separate exposures to D D T was s whereas it was heavy in the non

resistant strain In spite of a much higher proportion of the latter exposed to D D T, only a few were left alive for dissection All the groups of mosquitoes were dissected on the same day particularly for the determination of sporozoite infection of the salivary glands after the normal incubation period

Experiment 2 —Each group of the resistant and non resistant strain was given four exposures, the first immediately after infecting blood meal during the night and the subsequent three on alternate days The dosage of D D T was 200 mg per sq ft in all the cases and the period of contact was 40 minutes for each strain in the first exposure but in the subsequent exposures it was increased to one hour in the case of the resistant strain and decreased to 20 minutes in the non resistant strain so as to get a fair number of the mosquitoes for dissection after the incubation period of the parasite in the mosquito

Experiment 3 —Resistant females which had fed on a naturally infected sparrow were exposed to D D T as above for one hour once daily for the first four days Some mosquitoes of the same stock which had fed on the same sparrow were not exposed to D D T but kept for comparison

Experiment 4 —In this experiment 300 resistant *C fatigans* females were first exposed to 200 mg of D D T per sq ft for as long as six hours and then on release, immediately given an opportunity to feed on an infected sparrow, during the night The following morning 24 were up including 14 fully engorged females All these engorged specimens remained alive until dissection

Data concerning the foregoing experiments are set out separately in Table I

The results of comparative infections indicate that mere acquisition of resistance in *C fatigans* was not accompanied by any concomitant change in its susceptibility to infection with *P relictum* Both the resistant and non resistant strains were about equally infected up to the sporozoite stage

The effect of exposure to D D T, if any, on the development of sporogony cycle was not reflected in resistant or in non resistant strains of *C fatigans* as measured by the results of comparative infections Sporogony cycle was completed in a normal manner in resistant *C fatigans* in which the mechanism responsible for aborting or counteracting the lethal action of the toxicant was activated by one sublethal and three lethal exposures to D D T on alternate days which covered the entire incubation period or by four lethal exposures once daily during the early stages of the parasite development Likewise the results were similar in non resistant *C fatigans* after exposure to sublethal doses of D D T

There was no modification of the host parasite relationship when resistant *C fatigans* were subjected to a lethal contact with D D T for as long as six hours

preceding infective blood feed The presence of absorbed D D T in the surviving specimens did not seem to operate against the conjugating gametes or ookinetes that were being then formed in the stomach of the mosquitoes In other words acquisition of infection was not inhibited

TABLE I

Infection with P relictum *in D D T resistant and non resistant strains of* C fatigans *exposed to D D T*

Experiment number	Exposed or not	*C fatigans* Resistant strain: Number dissected	Gut positive	Glands positive	Total positive	Per cent total positive	*C fatigans* Non resistant strain: Number dissected	Gut positive	Glands positive	Total positive	Per cent total positive
1	Exposed	13	—	7	7	54	2	—	1	1	50
	Unexposed (comparison)	11	—	6	6	55	7	1	3	4	57
2	Exposed	21	—	8	8	38	11	—	5	5	45
	Unexposed (comparison)	21	2	9	9	43	14	—	6	6	43
3	Exposed	51	5	25	30	59	—	—	—	—	—
	Unexposed (comparison)	33	1	18	19	58	—	—	—	—	—
4	Exposed	14	3	5	6	43	—	—	—	—	—

Details —

Experiment 1 Two exposures of 40 minutes each, the first within 12 hours and the second on third day of the infective blood meal in both

Experiment 2 First exposure of 40 minutes immediately after infective blood meal followed by three separate exposures once every other day, of one hour each for resistant *C fatigans* and of 20 minutes each for non resistant *C fatigans*

Experiment 3 Four exposures of one hour each once daily, commencing from the first day of infective blood meal

Experiment 4 A single prolonged exposure of six hours preceding infective blood meal

Note 1 Resistant *C fatigans* were of Generation 43 in Experiment 1 and of Generation 44 in Experiments 2 to 4

2 Dosage of D D T was 200 mg in acetone per sq ft in all exposures

3 Usually only salivary glands were dissected for sporozoite infection In a few cases guts were also examined, particularly if glands were found negative

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DEVELOPMENT OF SPOROGONY CYCLE OF HUMAN MALARIA IN RESISTANT AND NON-RESISTANT STRAINS OF *A FLUVIATILIS*

Experiment 1 —Resistant and non resistant *A fluviatilis* were caged separately in screened bamboo rings and applied to a gametocyte carrier of *P vivax* All the mosquitoes could not be fed on the donor who on account of tender age (three years) would not tolerate mosquito bites The blood fed mosquitoes being small in number, were not exposed to D D T

Experiment 2 —One lot of resistant and another of non resistant strain were fed simultaneously on a crescent carrier * Here again, the mosquitoes were not exposed to D D T, in the hope of utilizing them for a neuro-syphilis case under the treatment of the Medical Officer, Government Hospital, Mettupalaiyam, South India This, however, did not materialize The results of dissection of both the experiments are shown in Table II

TABLE II

Infections with human malaria in D D T-resistant strains of A fluviatilis

Experiment number	Species of Plasmodium	*A fluviatilis*									
		Resistant strain					Non resistant strain				
		Number dissected	Gut positive	Glands positive	Total positive	Per cent total positive	Number dissected	Gut positive	Glands positive	Total positive	Per cent total positive
1	*P vivax*	49	2	2	3	6					
		*20	0	0	0	0	*14	0	0	0	0
2	*P falciparum*	[illegible]	4	18	21	40	[illegible]		39	39	52

Note 1 In both the experiments mosquitoes were not exposed to D D T
*2 Partially fed

It would appear that both the resistant and non-resistant strains of *A fluviatilis* were almost equally susceptible to infection with human malaria

DEVELOPMENT OF SPOROGONY CYCLE OF *P GALLINACEUM* IN NON-RESISTANT STRAIN OF *ÆDES ÆGYPTI* AFTER EXPOSURE TO D D T

Experiment 1 —In this experiment, mosquitoes were divided into three groups Females in group (*a*) were first fed on an infected fowl and then exposed to 25 mg of D D T for five minutes Out of 300 engorged females, 227 (or 76 per cent)

* Thanks are due to Dr A Kanagaraj Medical Officer Government Hospital Mettupalaiyam, South India for according permission to feed mosquitoes on this patient.

were found to have died the following day In group (*b*) females were first exposed to D D T as in group (*a*) and then given a chance to feed on the same infected fowl Very large numbers of mosquitoes were used because only a small proportion of the excited females could pierce the skin and take a blood meal The third group (*c*) which was not exposed to D D T was kept for comparison

Experiment 2 —In this experiment, *Ædes ægypti* females were exposed to D D T (25 mg per sq ft) as gravids for three minutes The following morning mortality among these mosquitoes was found to be 83 per cent (166 out of 20 females)

The results of dissection of mosquitoes of the different groups of Experiments 1 and 2 are detailed separately in Table III

TABLE III

Infection with P gallinaceum *in non resistant strain of* Ædes ægypti *exposed to sublethal doses of D D T (25 mg per sq ft) for five minutes*

Experiment Number	Conditions of experiment	Number dissected	Gut positive	Glands positive	Total Positive	Per cent total positive
1*a*	First given infective blood meal and then exposed to D D T	36	—	19	19	53
b	First exposed to D D T and then given infective blood meal	19	—	10	10	53
c	Comparison (unexposed)	21	—	10	11	52
*2 *a*	Exposed to D D T as gravids	24	19	14	19	79
b	Comparison (unexposed)	26	16	10	16	62

*Period of exposure only three minutes

It will be seen that a sublethal exposure to D D T of *Ædes ægypti* preceding or succeeding infective blood meal or in a stage of gravidity was found to have no effect on the development of *P gallinaceum* inside the mosquito host The index of infection was practically the same in all the groups of *Ædes ægypti* whether exposed to D D T or not

Experiment 3 —This experiment was started with *Ædes ægypti* most of which had recently become infected with sporozoites of *P gallinaceum* in the salivary glands About 75 of these females were exposed to 25 mg of D D T per sq ft. for five minutes

As soon as the exposure was over, the mosquitoes were given an opportunity to feed on a normal fowl (G 79) enclosed suitably inside the cage The mosquitoes, with developing symptoms of D D T poisoning were unable to penetrate the skin for a blood feed until after an hour when one female had become engorged This was dissected immediately and it showed a moderate sporozoite infection of the salivary glands Again, one hour later, the same fowl was bitten by three

mosquitoes in the course of 25 minutes, of which two were found infective At this point feeding was discontinued The normal fowl (G 79) was thus inoculated with sporozoites by bites of three known infective specimens which succeeded to obtain a blood meal after exposure to D D T

Another group of infected mosquitoes from the same stock was exposed to
A new normal fowl
quitoes by holding it
bitten by two proved
infective mosquitoes one after 50 minutes and another after one hour of the exposure

Both the normal fowls (G 79 and G 80), which were inoculated with sporozoites by bite of the infective mosquitoes after sublethal exposure to D D T, developed patent infection which ended fatally in one and in a spontaneous recovery of another The results demonstrate that a sublethal contact with D D T of infective mosquitoes did not render the sporozoites non infective to normal mosquitoes

The marked change in the biting potential of *Ædes ægypti* after exposure to D D T is noteworthy The same specimens of *Ædes ægypti* which would have immediately crowded and fed on the fowl in a few minutes were practically unable to do so after exposure to D D T

Experiment 4 —Mulligan *et al* (1940) have reported that sporozoite agglutination in high dilutions of malarial serum is a specific reaction This test was made use of to find out if sporozoites in salivary glands of *Ædes ægypti* had undergone any change after exposure to 25 mg of D D T for ten minutes Sporozoites from heavily infected specimens with self amputated legs and almost at death point, were dissected in different dilutions of homologous chronic serum The results suggest that sporozoites in highly paralyzed *Ædes ægypti* were not impaired antigenically

Inoculation of sporozoites from a highly paralyzed specimen into a normal fowl (G 81) caused patent infection after an incubation period of eight days, showing thereby that the sporozoites were infective The parasites reached their peak on the fourth day and disappeared from peripheral circulation on the seventh day

VIABILITY OF *P GALLINACEUM* IN INFECTED FOWLS POISONED WITH ORAL ADMINISTRATION OF D D T

Having demonstrated that the development of malaria parasites in resistant
osure
fowls,
non
who
estimated biologically the effects of B H C and D D T in the bovine blood by feeding arthropods on treated animals The two experiments carried out are described below

Experiment 1.—One normal fowl was inoculated with the blood of a fowl harbouring chronic infection. When infection first became patent, the fowl was given D.D.T. in olive oil by mouth at the rate of 100 mg. per kilogramme of the body weight for three days in succession. On the fourth day, the fowl began to develop early symptoms of D.D.T. poisoning and its blood picture revealed a number of male and female gemetocytes. On the same night when the fowl was in convulsions and prostration, it was placed bodily inside a cage containing large numbers of *Ædes ægypti* which became engorged in a short space of time. Soon after blood feed, most of the mosquitoes began to show toxic symptoms. In some specimens, the symptoms deepened and they fell down in the cage. After about 24 hours, more than half the females were dead. A few females which survived to complete the extrinsic incubation period, were dissected for finding out oocysts and sporozoite infection. All the 12 specimens were found infected with both oocysts and sporozoites. These sporozoites were normal in appearance in fresh and stained preparations. One normal fowl which was bitten by two infective specimens developed infection on the ninth day and died of malaria seven days later.

It would appear from the foregoing that in a normal fowl poisoned with D.D.T., the parasites multiplied and produced viable gametocytes which on being ingested by mosquitoes resulted in the production of sporozoites which in turn were proved to be infective to a normal fowl.

Experiment 2.—A normal fowl was inoculated with blood from the fowl with chronic infection. Before infection became patent, the fowl was given D.D.T. in olive oil as in the above experiment on three consecutive days. For some unknown re...
but died on
in the peripl...
the density of gametocytes was adequate the fowl was exposed to the bites of *Aedes ægypti*. The engorged females were slow in developing sysmptoms of D.D.T. poisoning. After about four hours most of the mosquitoes were unquestionably irritated in varying degrees. The surviving females showed 85 per cent infection of salivary glands with sporozoites (17 out of 20 dissected).

DISCUSSION

It is well known that certain species of mosquitoes have developed resistance to D.D.T., particularly in areas where D.D.T. has been used extensively and intensively in massive doses. This insecticide resistance may be slight so that mosquitoes are still killed by the insecticide or may have reached a stage where D.D.T. is of little or no practical value in mosquito control. The importance of the development of resistance, particularly in a vector species, would seem to depend largely on whether the ability of a resistant strain to withstand the doses of D.D.T. which would kill a non-resistant strain of the same species, would also operate adversely on malaria parasites in an infected mosquito. In discussing the possible effects of residual insecticides on the interruption of malaria transmission Gabaldon (1953) observes: 'If physiological resistance appears, its importance may depend on the fact that the sorbed insecticide may injure or not

he malaria parasite in any of its stages in the mosquito a fact unknown at the present time The same author again records Nobody knows what happens to oocysts or to sporozoites inside slightly intoxicated mosquitoes

On the basis of data on hand it is evident that mere acquisition of D D T resistance which was high in *C fatigans* and low in *A fluviatilis* did not result in any concomitant change of the vectorial capacity of these two species Resistant and non resistant *C fatigans* which originated from the same parent were almost equally infected with *P relictum* Similarly resistant and non resistant strains of *A fluviatilis* showed no difference in their susceptibility to infection with human malaria

It is also evident that activation of the mechanism of resistance in resistant *C fatigans* by lethal contact and in non resistant *C fatigans* by sublethal contact with D D T produced little or no effect on the development of sporogony cycle. Both the groups were infected with *P relictum* to about the same extent as were the comparison groups

It will be further observed that sporogony cycle was completed in a normal manner in resistant *C fatigans* which were exposed to lethal doses preceding infective blood meal or thereafter during the early or entire extrinsic incubation period

Experiments with *P gallinaceum* indicate that a sublethal exposure to D D T had no effect on the parasite in any stage in *Edes ægypti* and that when D D T was fed orally to fowls the parasites multiplied and gametocytes remained viable

Finally it would also appear that if contact with D D T resulted in any change physical or chemical in the body of an infected mosquito the malaria parasites were not apparently influenced by it in their natural environments

It is not known whether D D T absorbed by mosquitoes found its way to the [illegible]

SUMMARY AND CONCLUSIONS

1 The acquisition of D D T resistance by *C fatigans per se* had no apparent effect on its vectorial efficiency Both the resistant and non resistant strains originating from the same female were about equally infected with *P relictum* up to the sporozoite stage There was no change in the host parasite relationship when the mechanism of resistance was stimulated by exposing the resistant strain to lethal doses of D D T preceding infective blood meal or thereafter during the early or entire extrinsic incubation period Sporogony cycle was completed in a normal manner in resistant and non resistant strains irrespective of the exposure to D D T

2 Resistant and non resistant strains of *A fluviatilis* were almost equally susceptible to infection with human malaria Resistance in *A fluviatilis* was of course low but it was clear cut

3. A sublethal exposure to D D T. of *Ædes ægypti*, preceding or succeeding infective blood meal or in a stage of gravidity, was found to have had no effect on the acquisition of infection with *P. gallinaceum* or its subsequent maturation to sporozoites Exposure of the infective females did not render the sporozoite non-infective to normal fowls

4 Oral administration of D.D.T. to fowls infected with *P. gallinaceum* did not inhibit the multiplication of the parasite, nor did it have any apparent effect on the viability of gametocytes.

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POLICY IN RELATION TO MALARIA CONTROL

BY

S R CHRISTOPHERS

(August 1 19)

How important is policy in measures directed to the control of malaria in a country? By policy is meant all that goes to the thinking out of what should be done It includes what it is desired to do what it is possible to do and how this last can best be done It is sometimes not very clearly thought out often based on imperfect information and with the best intentions it may not be the best that could be adopted One thing it very commonly lacks is adequate provision to show what results have been achieved It is therefore worthwhile to give careful thought to what it is hoped to do how it can best be done and how if it is done it can really be known to be done

What it is hoped to do may be the elimination of malaria as a human disease To have any relation to reality such hope must be more specific in time and place There are two words in use in the fight against malaria viz control and eradication those whose expectations are aimed high prefer eradication those less optimistic use the word control As in many human affairs a great deal depends on the particular circumstances and what is reasonable to hope in some circumstances would be unreasonable in others Whatever the objective however whether control or eradication much the same techniques must be used Malaria is almost unique as a disease in the great varieties of ways in which it may be attacked and the number of techniques that can be used in doing so The important point that policy has to decide upon is which of these techniques to use It may be useful to indicate briefly what these techniques are

Early control measures, following upon Ross s discovery of the mosquito transmission *of malaria were almost entirely based on action taken against the* breeding places of Anopheles The only important rivals to such measures were communal quinine prophylaxis and screening Discovery of paris green as a more efficient and easily handled larvicide and the work of Malcolm Watson in Malaya exploiting the use of drainage and other methods of larval control together with the conception of species sanitation appeared to show that control through antilarval action was possible and that where it could be carried out it was the method of choice as being the most fundamental Other measures such as the

trapping and spraying or fumigation of adults, use of communal quinine and protection took their place as measures to be used where antilarval work was unsuitable or as supplementary measures of securing success So successful in

of merely reducing Anopheles eradicating once and for all s method were that the area must not be too great, though it was not necessarily restricted to an island, and considerable areas were treated on this basis

Some operations of this kind have been highly successful *e g*, *Anopheles gambiae* which appeared to have invaded Brazil from Africa and there had occasioned serious epidemics of malaria, as a result of a determined and systematic attack launched by the Rockefeller Foundation in association with the Brazil Government under Doctors Soper and Bruce Wilson was completely eradicated from North East Brazil and up to the present (Russell, 1955) Brazil has remained free from this species Another successful anti *gambiae* eradication operation has been carried out in Upper Egypt (invaded area 4,270 sq miles and population some three million) In Sardinia, at a total cost of 12 million dollars and with the assistance of some thousands of scouts, an attempt was made to eradicate the vector species But though malaria was eradicated the operations were not completely successful in eliminating the indigenous species of Anopheles In Cyprus, an island with endemic malaria (spleen rate about 25 per cent), there was an example of the use of the new insecticide D D T as a larvicide Here also an attempt to eliminate the indigenous Anopheles was unsuccessful, though as a result malaria was much reduced

In the first world war antilarval control, with in addition quinine prophylaxis where larval control was impractical or required supplementing, was still the recognized m

and other are

Nevertheless

in the second world war

In the period between the two wars, two things revolutionized ideas regarding control These were the discovery of new more and more effective synthetic antimalarial drugs and the results from the new insecticide D D T used in residual spraying Drug prophylaxis through mepacrine, now as a result of the previous war pushed as a prophylactic measure with the full and effective support of the military commands was practically the answer to malaria control in troops The new and powerful insecticide D D T, used first as a larvicide and eventually along with a number of related compounds in residual spraying has been so dramatically successful that many have considered it the final answer as to how malaria can be fought

With this brief resume of the present position with respect to various forms of techniques used against malaria we may usefully examine some considerations that affect policy It will be most convenient to do so chiefly in relation to experience in India

AREA AND POPULATION

In Table I, are given the area population and persons per square mile in a number of tropical malarious countries

PLATE VIII



B Colon I S RICKARD CHRISTOPHERS A . . R I
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TABLE I *

Area, population and persons per square mile in a number of tropical malarious cuontries

Country	Area in square miles	Population	Persons per square mile
An English county (Cambridge)	492	177,000	360
Trinidad	1 860	678 000	366
Cyprus	3,570	505,000	140
Sardinia	9,300	1,220,000	131
British Guiana	83 000	450 000	5
Venezuela	352 000	5 323 000	15
,, (treated area)	69 000	2,431,000	35
Bolivia	415,000	3,788 000	9
Gold Coast	24 000	2,223 000	92
Nigeria	373 000	31,200,000	83
Belgian Congo	910 000	12,115 000	13
Tropical Africa as a whole (From 15° N to the level of Beira)†	6 000,000	60,000,000	10
Pakistan	364,700	75,840,000	207
India	1,143 000	356 179,000	312

* Data, except for tropical Africa as a whole, from Whittaker s Almanac, 1955

† Area for tropical Africa has been measured from map and given approximately The figure for population is probably an under estimate

Such a list serves to show the relative scale of operations that would be required for these countries and emphasizes the special cases of India and some tropical African countries

ECONOMIC STATUS

There will almost certainly be a great difference in what a prosperous and perhaps largely europeanised country can do as compared with a relatively poor country much of the population of which may be living in rural or even jungly conditions Between two such, the whole question of malaria control differs enormously and, except as experiment for some particular purpose, what one might almost term smash and grab operations are not usually the most suitable in the latter circumstances

VITAL STATISTICS

One point that it is very necessary to know in a country where the question of action against malaria arises is how much malaria there actually is Normally it is assumed that this will be shown by the vital statistics, as also whether any steps that have been taken have produced the desired result Unfortunately, where the

thing and cannot be expected to be accurate In general, vital statistics are of little use except in very special cases in determination of malarial incidence Hospital records in such countries often represent only a fraction of the real number of cases of a disease Medical men may be, and usually are, so small in proportion to the population in rural and jungly areas that any attempt to arrive at an estimate of the effect of operations on a large scale through medical diagnosis would be liable to grave doubt To do so from films sent in to headquarters might be extremely misleading Unless a good system of returns of death is in existence or there is a sufficiency of effective dispensaries any real estimate of the amount of malaria would require expert investigation

DISTRIBUTION OF MALARIA

It is not usually that a country is uniformly malarious or even that there *are not extensive areas where malaria is not a serious problem In India there are* some considerable areas that come under the designation of healthy In such areas malaria is often restricted to small foci of infection where conditions happen to be favourable to the disease Other tracts may be hyperendemic, *i e*, malaria is no longer an occasional disease, but one in which infection in childhood is universal, or almost so and adults are largely immune Even the children though infected, often show little evidence of being

as seen in some primitive tribes it may be difficult

child mortality On these accounts the urgency

action under such conditions has been considered by some authorities to be doubtful It is a matter of opinion with little factual evidence to go on Such areas may be quite extensive and have been mapped and much studied in India In other forms of high incidence communities may be in a miserable state of perpetual illness from malaria and in need of urgent relief These may be the conditions in communities colonizing new areas and perhaps labour connected with importnt industries or projects Without some system of ascertaining what areas and

EPIDEMIC MALARIA

One form of malaria, that termed seasonal epidemic, or when very severe fulminant malaria is especially important Its characters are sudden onset with

almost universal infection and high death rate. Such epidemics in India occur only at intervals of a decade or so, between which times it is characteristic that malaria is of relatively low incidence. It has been shown by Gill who has made a very thorough research into the nature and origins of such epidemics in India and Ceylon to be a phenomenon related to a normal low malaria incidence with decreased immunity followed in certain years by unusual and still not very well understood conditions favourable to malaria. In the year 1908, a great

to this danger of flooding and appropriate measures on a large scale to mitigate such effects have been taken. Whether on this account or not, these epidemics which usually occurred about every eight years as far back as records go have never since occurred on a like scale. Study of relatively small affected areas has shown that the measures which can be adopted are mainly organized arrangements for treatment and free drug distribution. Areas liable to such epidemic effects have been mapped and it has even to some extent, through studies of the spleen rate and other factors, been possible to foretell likely affected areas.

STAFF

For operations on any scale trained staff is a serious problem. This must necessarily include, besides labour and operators for whatever method is adopted, a sufficiency of trained malariologists to direct and supervise operations. During the last war the sudden call for personnel to equip antimalarial units operating in the was largely met from the Malaria Institute of rge organization where training was and ha the years of the war the Institute supplied for this purpose 555 trained malaria officers, 426 trained personnel and 87 engineers that had received malaria training.

ORGANIZATION

It will be clear from this brief account that organization and research are a very essential part of anti-malarial work. Without them measures must be taken blindly and proof that anything has been achieved may leave much to be desired. Whilst all out attacks can be made on malaria where large funds are available and circumstances favourable, it would seem these are not most suited to undeveloped areas or countries such as many are in the tropics where malaria assumes a variety of forms and degrees of intensity. What seems to be more needed in this case, especially where the country at issue is large, is some permanent organization where investigation and control can work hand in hand, its staff able to cover all the necessary fields of expert knowledge, familiar with field conditions, expert in malaria techniques, with access to government and supported on a scale proportionate to the task committed to them. In India in the course of the last

thirty years or more there has been developed a centre of malaria research and control on a scale and with an output of results that can safely be said to be second to none other in the world, *viz*, that now named the Malaria Institute of India

Only very brief mention can here be given of the history and work of this Institution A very instructive and complete account, however, will be found given by Covell in two communications, the first dated 1938 in Vol 1 of the *Journal of the Malaria Institute of India* giving the history and work of the Malaria Survey of India (1927-1937) and the second dated 1947 in Vol I of the *Indian Journal of Malariology* giving the history and work of the Malaria Institute of India up to that date Up to 1909, there was in India no organized plan for malaria research or control In that year, however, proposals were made for a malaria organization for India by Lieut-Colonel J T W Leslie, Sanitary Commissioner with the Government of India, whose far sighted policy was also responsible for the building up of the Bacteriological Department of the Government of India in which was combined the running of the large Central and Provincial Laboratories and much else The scheme included a General Committee (with the Minister as President) with a delegate from each Province and Provincial Committees to obtain information and supervise local enquiries A part of the scheme was the Central Malaria Bureau (1910-1916 and 1919 1927) At the Bureau were instituted a reference library on malaria, collections which later formed the basis for work on the mosquitoes of India, and other activities aimed at advancement of malaria work throughout India and Burma The Bureau maintained close connection with researches and surveys carried out by the Provincial Malaria Officers many of whose names have been then and later familiar in the literature It also held an annual class of instruction for medical officers taking up malaria work in which both field work and necessary laboratory techniques were undertaken Unfortunately the first world war necessitated the calling up of most of the Provincial Malaria Officers for duty in different theatres of war and the organization was for a time in abeyance Proposals, however, in 1924 for a renewed organization led in 1927 to the formation under the Indian Research Fund of the Malaria Survey of India with Lieut-Col (now Brigadier) J A Sinton as Director At first located at Amritsar, a city severely affected by the 1908 epidemic, it was later moved to Karnal where operations were in progress, but later at the director s suggestion to the present headquarters in Delhi In 1938, at a meeting of the Indian Research Workers Association, the Government of India agreed to finance the now greatly enlarged organization, which under the name of the Malaria Institute of India continued work under the directorship of Col (now Major General Sir Gordon) Covell, followed on his retirement in 1947 by Lieut-Col Jaswant Singh Throughout these years innumerable surveys have been made of different areas in India, control measures carried out and in almost every field of malaria control practical measures and techniques perfected Some idea of the extent and variety of the work carried out may be gathered from the list of papers published in the Journal of the Institute In recent years a great deal of study and experimentation has been given to residual spraying and its effects on which many papers will be found in the Journal Should residual spraying be found to give all that it promises one may safely leave its full exploitation in control of malaria to the present director and his expert staff That there

is no lack of initiative is shown by the recent formation of an associated Society with its own Bulletin, viz, the National Society of India for Malaria and other Mosquito Borne Diseases of which Lieut Col Jawsant Singh is the President and the objects of which include work on filariasis in India which causes much sickness and is a mosquito borne disease

Quite recently I have seen the announcement that a Malaria Institute has been established under the directorship of Dr D Bagster Wilson in tropical East Africa the East African Malaria Unit of the East Africa High Commission having become the East African Institute of Malaria and Vector Borne Diseases Such a step has very much to recommend it

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DEVELOPMENTS IN MALARIA CONTROL METHODS DURING THE PAST FORTY YEARS

BY

SIR GORDON COVELL M D D P H

(Jul 4 19

A PERIOD of 40 years has been selected for this review because it corresponds approximately with the writer s own experience of malaria and its control The developments which have evolved during this time in the methods used to combat the disease may be considered under the headings of (a antimosquito measures and (b) chemotherapy

ANTIMOSQUITO MEASURES

During the first half of the period the measures adopted were directed almost exclusively towards the destruction of the aquatic stages of the mosquito the egg larva and pupa usually referred to as antilarval measures Some of the earlier campaigns such as those undertaken in Malaya Ismailia Cuba and the Panama Canal Zone, were very successful They were costly but in each case important financial considerations were at stake and the expenditure was amply repaid by the improvement in health which resulted particularly among the labour forces employed

In India the prosecution of antilarval measures received a serious setback from the comparative failure of the campaign undertaken at Mian Mir, later known
drainag
and in
largely
from outside the protected area The campaign was further discredited when the great regional malaria epidemic of 1908 one of the most severe ever experienced swept over the Punjab Mian Mir lay within the epidemic area and many cases occurred among the troops stationed in the cantonment and their families

During the next 25 years antilarval measures were practised with some success in various urban areas in tea coffee and rubber plantations and in connection with large scale engineering projects Following Bentley s survey of 1909-1911 a Special Malaria Department was created for Bombay City and a

number of antilarval measures were put in force, directed chiefly towards the prevention of mosquito breeding in wells and cisterns, the favourite breeding places in Bombay of the vector, *A stephensi* As a result, the malaria rate was greatly diminished, so much so that the local authorities decided that the measures could be relaxed Accordingly in 1918 the Malaria Department was disbanded, but the meagre staff remaining proved entirely inadequate to cope with the situation Covers and trap doors of wells and cisterns were removed or allowed to get into disrepair and numbers of wells which had been sealed were re-opened The incidence of malaria began to increase and in 1922 the heads of 40 commercial houses sent in a petition to the Corporation drawing attention to the prevalence of the disease in the city and to its harmful effects on commerce In 1923, the Malaria Department was reconstituted, but much of the work previously accomplished had to be re-done in 1924, the disease was again very prevalent in Bombay and there were a number of cases among the crews of ships berthed in the docks A Central Malaria Committee was appointed and the staff increased, but malaria continued to be a serious problem and it was decided to hold another survey of the whole island This survey, which lasted six months and involved the examination of more than 30,000 children, was carried out by the writer in 1928 The recommendations then put forward, which were directed solely towards the prevention of mosquito breeding, were implemented with excellent results

In Assam, antilarval work was carried out in a number of tea estates under the auspices of the Ross Institute, notably by Ramsay in and around Labac An interesting development here was the growing of dense vegetation over ditches, streams and swamps to prevent mosquito breeding This measure was very successful for some years, but in the course of time the bushes used for shading began to invade the tea, necessitating the employment of extra staff to keep it cut back Eventually in many instances estates reverted to open drains and oiling for the control of mosquito breeding A similar course of events occurred in Malaya, where extensive subsoil draining was installed in rubber estates Here again the measure was at first successful, but eventually the roots of trees grew down in between the tiles in search of water and choked the channels, so that an open space $1\frac{1}{2}$ times the height of the trees had to be left on each side of the pipes Since a rubber tree may grow to a height of 60 feet or more, a large proportion of the plantation was thus put out of action In many estates the subsoil pipes were pulled up and substituted by open drains and oiling

Mention may be made of two engineering projects in India whose construction was made possible solely by
the Sarda Canal Headworks
Provinces, and the building c
Nagpur Railway The construction of the latter project was held up for 40 years owing to the prevalence of intense malaria, the incidence of the disease among the survey parties being so high that the first three were unable to complete their task, while the fourth succeeded only when every engineering post in the party was duplicated The construction of the railway was finally made possible by the work of the late Major Senior White, Malariologist to the railway, who instituted rigid antilarval measures in and around the camps in which the labourers were concentrated

During this period, the chief methods employed for the control of mosquito breeding were drainage and the application of various kinds of oil to water collections. A notable advance was the introduction as a larvicide of paris green, following the demonstration of its value in the field by Barbar and Hayne in 1921. From this period until the advent of D D T paris green was used very extensively in large scale antimalaria campaigns throughout the world. It was the principal method employed in the Brazilian campaign of 1939 40 which resulted in the eradication of *A gambiæ* from that country.

The experience gained during the earlier antimalaria campaign in India and elsewhere showed that the disease could probably be controlled anywhere by antilarval measures, *provided that sufficient funds were available for the purpose.* Under urban and industrial conditions where the population at risk was concentrated in a limited area and where its potential output was economically productive, it could usually be demonstrated that the cost of malaria to the community was considerably greater than that of effective control even by the measures then available. It was the control of *rural* malaria that for so many years proved an insoluble problem to the health authorities of tropical and subtropical countries. Here the population instead of being concentrated in compact areas is scattered ... lated groups of houses ... harbours innumerable ... was indeed controlled in rural areas in certain instances as a demonstration project but only at a cost far greater than any sum which the local authorities could afford. Under such circumstances the only way of ameliorating the condition was to provide treatment for the sick, a palliative rather than a control measure.

This was the position as late as 1936 when the publication of the remarkable results achieved in South African villages by the spray killing of adult mosquitoes with pyrethrum insecticides at a moderate cost encouraged the hope that here at last was a weapon which might prove practicable for the control of malaria in rural India. Just at that time a comprehensive scheme of malaria control was being put into operation in Delhi urban area which covers about 75 square miles of country. The quarters occupied by certain selected communities of Government employees located in particularly malarious sections of this area were regularly sprayed throughout the malaria season. The results were remarkably good and in one set of quarters the malaria rate was reduced to 1 4 per cent, a figure of 45 per cent being recorded in adjacent quarters which were left unsprayed. The method was immediately recommended for use throughout India for personnel such as police, railway, forest or other government employees and labour forces in estates, mills and other industrial enterprises. It was at first thought that its usefulness would be limited to such conditions but in 1937 it was tried as an experimental measure in t ... extended to a number of ... experimental work on the ... Unit of the Rockefeller Foundation International Health Division in certain villages in southern India during the period 1938 41. The first large scale routine application of this measure in Indian villages was, however, carried out in Mysore State.

When the Bombay State Malaria Organization was created in 1942, the spray-killing of adult mosquitoes with pyrethrum insecticide became an important feature of the control programme in Kanara District   Early results in this area were somewhat disappointing, [illegible] based on a series of patient res[illegible] malaria rate   In September 1945, [illegible] imported into India for military purposes was made available to the Bombay Malaria Organization for field trials   From then onwards the spray killing of mosquitoes with residual insecticides became the main feature of the campaign, which was progressively extended to cover the whole of the malarious parts of the State

In the same year a large-scale project was launched in Venezuela with the object of eradicating malaria from the entire country by D D T residual spraying and similar campaign was inaugurated in British Guiana   Since then, D D T spraying projects have been carried out in Brazil Argentina, Bolivia, Peru, Ecuador, Columbia and French and Dutch Guiana   In the United States a joint programme for eradicating malaria was also launched in 1945, with the result that the disease has now practicall [illegible] Large scale campaigns are in progress in Italy [illegible] Cyprus, Greece, Mauritius Ceylon, Thailand, t[illegible]nd Iran, as well as in India and Pakistan   In all these projects spraying with residual insecticides has been the chief and in many cases the sole, antimalaria measure employed

It is interesting to recall that the systematic destruction of adult mosquitoes was practised in the Panama Canal Zone as early as 1908, the first to use it being W R Procter, a sanitary inspector   It was done by negro labourers armed with chloroform tubes and acetylene lamps   Mosquitoes were also caught in wire gauze traps, placed over the windows   These measures met with considerable success in reducing the malaria rate   The destruction of hibernating adult mosquitoes by hand catching was also practised in Holland from 1920 onwards, and in 1926 pyrethrum sprays were introduced for this purpose   It was this work in Holland, largely inspired by the insistence of S P James on the importance of destroying the infected mosquito and thus interrupting transmission, which formed the basis for the successful campaign in South Africa alluded to above

CHEMOTHERAPY.

During the first decade of the period under review the only drugs available for the prophylaxis and treatment of malaria were the cinchona alkaloids, of which the most commonly used was quinine   It was customary to give the drug over an extended period, beginning with 20 to 30 grains daily for seven to ten days, this was usually followed by a similar dose twice or thrice weekly for several weeks or even months   During the first world war, quinine was given to the troops in Macedonia in enorm[illegible] after the [illegible] relapse [illegible] of 1,350 grains   Another, known as a sterilizing course, [illegible]

of quinine orally plus 30 grains intramuscularly daily for 12 days, 60 grains orally for two days, and 20 grains orally for the following two weeks, a total of 1,180 grains

The numerous investigations conducted between the two world wars, notably those sponsored by the League of Nations Malaria Commission together with experience gained during the treatment of neurosyphilis with malaria therapy, resulted in the general adoption of comparatively short courses of treatment for malaria It was established that any dosage of quinine exceeding 30 grains daily not only fails to affect the course of the disease, but is also detrimental to the health of the patient, and that to extend the course beyond seven days has no effect on the relapse rate

The evolution of the synthetic remedies now so largely used in the treatment and prophylaxis of malaria makes an interesting story Quinine is an effective drug for terminating the clinical attack in most malarial infections and it is doubtful if any of the synthetic drugs now in use would have been developed had not the Germans been deprived of all sources of quinine during the first world war It was the necessity for finding an effective substitute for quinine which inspired the researches which led to the synthesis first of plasmochin (pamaquin) and later of atebrin (mepacrine)

Up to the time when this work was planned, all attempts to synthesize quinine had failed, but Guttmann and Ehrlich, many years earlier had discovered that methylene blue stains, and, therefore, presumably penetrates, the malaria parasite and had observed some abatement of clinical symptoms in patients suffering from *vivax* infection to whom the dye had been administered With these experiments in mind, a team of German scientists embarked on a line of research which was destined to have far reaching consequences They introduced a basic side chain into the formula of methylene blue, and found that one of the resulting compounds had considerable activity against bird malaria It seemed likely that the activity of the quinoline [illegible] the introduction of a similar b[illegible] in the synthesis of pamaquin, [illegible] effective action against human malaria parasites

Pamaquin was found to have a powerful destructive action on the gametocytes of *Plasmodium falciparum*, a property not possessed by any of the cinchona alkaloids, another quite unexpected development was the demonstration in India by Sinton and Bird that when used in conjunction with quinine it effected a marked reduction in the relapse rate of *vivax* malaria In certain respects however, pamaquin proved unsuitable as a therapeutic agent, chiefly by reason of its relatively high toxicity and the fact that it has little action on the asexual erythrocytic forms of *P falciparum* The Germans therefore, embarked on further studies, they attached the basic side chain which had been evolved for pamaquin to other heterocyclic nuclei, and finally, in 1930, produced the acridine compound mepacrine

Mepacrine proved to have a powerful destructive action on the asexual erythrocytic forms of all species of human malaria parasite It possesses all the antimalarial properties of quinine, and against some strains of *P falciparum* it is considerably more active It has, however, the disadvantage of turning the skin yellow and of producing in certain individuals undesirable side-effects

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After preliminary tests on patients [illegible]
and later in England, pamaquin and [illegible]
series of field trials under the auspice [illegible]
afforded clear and decisive proof of the high suppressive action of mepacrine in all forms of human malaria, though some uncertainty remained as to the possible harmful effects of long continued administration When Indonesia fell to the Japanese in 1942, thus cutting off the supply of quinine to the Allies, steps were immediately taken to manufacture mepacrine in large quantities in both Great Britain and in the United States Mepacrine prophylaxis was rigidly enforced among the Allied troops operating in the South west Pacific and South east Asia Commands This measure resulted in effective control of malaria in both areas and played an important part in achieving final victory

The German programme of research on synthetic antimalarials had not ceased with the production of mepacrine They continued their investigations with the object of producing a drug with the same antimalarial properties but without its disadvantages Removal of the methoxy-bearing ring from the mepacrine molecule gave rise to resochin (chloroquine), a member of the 4-aminoquinoline group of compounds Preliminary tests of this drug on a small series of patients in a mental hospital in Germany were interpreted as indicating a considerable degree of toxicity, and further research was undertaken to counteract this supposed defect.

The second world war broke out while this work was still in progress and as field tests of the 4 aminoquinolines were as yet incomplete, the Germans adopted mepacrine as the standard antimalarial drug for their troops After the occupation of France supplies of chloroquine and of an allied compound, sontoquine, were made available to the French authorities for tests in North Africa, when this area was occupied by the Allies, stocks of these fell into the hands of the Americans, who were already engaged in a gigantic research programme in which more than 14 000 compounds were eventually tested for antimalarial activity

The Americans found that the early German tests of chloroquine had created an exaggerated picture of its toxicity, they also found it superior to sontoquine as an antimalarial drug It had the advantage over mepacrine of not causing discoloration of the skin, it was found to be in some respects more active than the latter drug and less likely to produce unpleasant side effects It was not used to any great extent during the second world war, but was soon afterwards adopted as the standard antimalarial drug for the United States Army Two other 4-aminoquinolines, amodiaquine (camoquin) and hydroxychloroquine (plaquenil), have similar properties and are claimed to be equally effective

During the latter half of the second world war, British chemists, adopting a new line of approach produced a biguanide compound, proguanil (paludrine) which proved to have remarkable antimalarial properties This drug acts on the pre erythrocytic forms of *P falciparum*, and is therefore, a causal prophylactic of infection due to this species of parasite, it is a good suppressive against all forms of malaria, it inhibits the late sporogonic forms of the parasite, so that mosquitoes feeding on a gametocyte carrier receiving therapeutic doses of the drug do not become infective, it has a lower toxicity than any other antimalarial drug known, and it can be produced at very low cost Its action on the asexual erythrocytic

orms of the malaria parasite is not sufficiently rapid to render it suitable for reatment of the clinical attack and its principal use is in prophylaxis Proguanil ias been used very extensively for this purpose among troops and civilian popula tions in Malaya and other parts of the Commonwealth during the post war years with excellent results

More recently another antimalarial drug of importance has been placed n the market *This is pyrimethamine (Daraprim) a member of the diamino* pyridine group It was synthesized in the United States though many of the

kely to be in prophylaxis It is active in very small doses and can be produced it relatively low cost

Proguanil and pyrimethamine share one grave disadvantage namely a endency to provoke resistance in parasites subjected to prolonged contact with ther drug in sub therapeutic dosage Cross resistance between the two drugs ias also been demonstrated It is not possible to forecast at this stage how far this phenomenon will affect their future use Fortunately no such tendency has yet been observed in respect of either chloroquine amodiaquine hydroxychloroquine nepacrine or quinine

Another important new antimalarial drug developed in the United States s primaquine one of the 8 aminoquinoline series The researches which led to ts production were inspired by the urgent need for preventing relapses of *vivax* nalaria in trooops returning from Korea It is claimed that the maximum olerated dose of primaquine is twice as high as that of pamaquin and that it is our times as active as the latter drug in the radical cure of *vivax* malaria Since ts adoption as a routine method of treatment the relapse rate among the United States personnel returning from Korea has fallen to less than one per cent

COMMENT

No student of malariology can fail to be impressed by the profound influence xerted by the exigencies of war on the development of malaria control measures during the past 40 years

The greatest advance in the conduct of antimosquito measures during this period was the introduction of D D T This compound had been synthesized as arly as 1874 but its insecticidal properties were not discovered until 1939 when wiss chemists were searching for a chemical which would destroy clothes moths D D T was first used on a large scale in the early years of the second world war against the Colorado beetle which threatened the Swiss potato crop at a time when military considerations had made the preservation of all foodstuffs of the utmost importance The need for a synthetic insecticide has been intensified by he shortage of pyrethrum the bulk of which was then grown in Dalmatia and Japan and in 1942 D D T was made available to the military authorities in Great Britain and in the United States It was used with great effect for the prevention of typhus during the Italian campaign and later in the war it was employed on a

large scale by the military authorities for the destruction of mosquitoes and other insect vectors of disease Although D D T was already in existence when the war broke out, the researches which demonstrated its possibilities as an agent for malaria control were inspired directly by military considerations

Wartime conditions had an even greater influence on the development of synthetic antimalarial drugs than on that of residual insecticides As noted above it was the fact that they had been deprived of the sources of quinine during the first world war which inspired the German researches which culminated in the production of pamaquin and mepacrine Chloroquine was evolved as a further development of the same line of research and its outstanding properties as an antimalarial drug were demonstrated by the Americans in the course of their wartime research programme The investigations which led to the production of proguanil were begun because the Allies in their turn were cut off from sources of quinine when the Japanese occupied Indonesia Finally, as already noted primaquine was produced in an attempt to evolve a safe substitute for pamaquin for the treatment of personnel returning from the Korean battlefront

Thus the wars which have devastated the world during the past 40 years have had at least one beneficial effect, in that they have stimulated the development of synthetic insecticides and drugs which bid fair to rob malaria of most of its terrors and perhaps even to lead to its eventual eradication from the globe

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THE NATIONAL MALARIA CONTROL PROGRAMME OF INDIA

A Review.

BY

B ANANTHASWAMY RAO

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(September 12 1955)

INTRODUCTION

AWARENESS of the enormity of the problem of malaria, both from the public health and the socio-economic points of view, has existed in India through several decades Indeed, it had been repeatedly demonstrated for over two decades in different States that it was feasible to control and prevent malaria efficiently and urban malaria even economically The social and economic betterment of communities in whom the malaria was controlled, was only too obvious Between 1946 and 1953, several States had carried out large scale successful antimalaria programmes with indoor residual spray of D D T in the rural areas At the close of the financial year 1952-1953, about 30 million people out of an estimated 200 million exposed to the risk of malaria, were being protected from the disease at an annual cost of 15 million rupees (Jaswant Singh, 1953)

The need for and the feasibility of a national programme for malaria control had been visualized as early as 1946 when the Health Survey and Development Committee recommended a nation wide effort It was, however, in 1952 that a plan was formulated as a part of the health development programme of the first Five Year Plan for the country The Indo-American aid made it possible to launch this first national health drive

THE PLAN

Extensive knowledge of malaria and methods of its control under widely differing epidemiological conditions involving several vectors, was a great help in the formulation of the Plan Although based on certain assumptions dependent on the data available, it was dynamic, capable of modifications as and when

necessary The plan is technically sound and has had necessarily to be an experiment in so far as its administration, organization and execution are concerned

Programme of India remains to date unique and the biggest in the world It is proposed to review this programme in retrospect and prospect after three years of execution

Based on the assumption that 200 million people of the country's population are exposed to the risk of malaria (with an estimated annual morbidity of 75 million and mortality of 0 8 million), the plan was drawn with a defined objective to protect the entire population at risk from further infection The emphasis of the plan would in retrospect appear to be mainly rural malaria control

The method of malaria control provided was to intercept the transmission
al insecticides in the dwellings (75 per cent
e or twice and rarely three times a year
total dosage of 200 mg of technical D D T
For over all calculation, an average house
was reckoned to have one thousand sq ft of indoor surface to be sprayed Each house was reckoned to have a population of five

The plan envisaged an operational phase of three years and a maintenance phase thereafter The financial implication of the plan during the years of the operational phase was estimated at Rs 1 505 lakh The major part of this, namely, Rs 772 7 lakh, was to be American aid in kind (transport, equipment, D D T), while the Government of India was to contribute Rs 227 3 lakh for the expansion of Malaria Institute of India and the provision of antimalaria drugs, locally produced insecticides and customs duty on material coming from abroad The United Nations International Children Emergency Fund gave Rs 15 lakh worth D D T The State Governments' contribution was estimated to Rs 490 lakh to cover the salaries of the staff employed and running expenses

The plan provided for the protection of 125 millions only out of the 200 millions estimated to be at risk The implementation of the programme was to be phased to set up the required organization in the different States for the protection of 75 millions in the first year of the plan and the full 125 millions during the second and third years Thereafter, it was expected that the tempo of the control operations would be scaled down to the maintenance phase It will be seen later that some changes from the original planning had to be made, even within the first three years

RESPONSIBILITIES

Direction, co ordination, over all supervision, training of staff, procurement and supply of equipment, transport and insecticides and final assessment were allocated as central responsibilities to be discharged by the Malaria Institute of India The States were to be responsible for the recruitment of staff, execution of the programme, immediate supervision and concurrent assessment of results

In accordance with the Constitution, Public Health being a State responsibility, it was necessary to circulate the plan and invite the concurrence of the States to participate in the national effort Each unit of the National Malaria Control Programme was designed to protect a population of one million and the States were requested to indicate the total number of units required to cover all the malarious areas in each, and the number they could support It was fully

organization as quickly as possible

IMPLEMENTATION

Saturday, December 13 1952, will be remembered as a landmark in the history of malaria control in India when the relevant operational agreement was signed in New Delhi, between India and the United States of America That agreement made it possible to equip and provide insecticides transport and equipment for 75 units in 1953-1954, each unit protecting one million population It was found necessary, however, by a second agreement in the same year to provide for 15 additional units, bringing the total for the first year to 90 This addition was made possible by the free grant of 400 tons of D D T by the United Nations International Children Emergency Fund In March, 1954, as a result … for 35 more units, … d to 136 to protect … been increased to 162 by allocating additional 26 units during 1955 1956

It would thus be seen that out of an original estimate of population at risk, namely 200 million, there still remain 38 millions requiring protection

Despite the fact that all details of planning and logistics of supplies, etc, were given due consideration, there were some inevitable birth pains Perhaps …

bottle necks of rail and … ok some considerable time for the transport, … imate destinations where they … d and willingness of all concern …

Some Government policy decisions and procedural formalities resulted in the supply of a few items of transport and equipment not suitable for use under the varied field conditions in the country The trucks, for example, were found to be too large for being manipulated underneath overhead railway bridges, etc The power sprayers were found to be unusable due to their huge size These difficulties were freely discussed at a conference of field workers and were got over by local initiative and rectified in subsequent procurement

The insecticide formulation (75 per cent water dispersible powder) received from America was from different manufacturers in that country In addition, the

periods of storage and transit for various consignments were different from one another When the first complaint was received about the difficulty of obtaining a good water suspension out of a batch of insecticide received in the country it became necesary to inspect and test every consignment of insecticide received at the different ports before distributing them to the various States Simple devices for testing of the insecticide formulations, as well as for rendering them suitable where found to be wanting in the required specifications, were quickly developed with the full cooperation of the U S Technical Cooperation Mission to India

BOTTLE NECKS

There was initial delay in the recruitment of staff both in the Centre and in the States on account of procedural formalities The latter have also been responsible for long delays in procurement of supplies It is time that necessary action was taken to see that such bottle necks are not allowed to interfere with the scheduled implementation of an emergency programme like the National Malaria Control Programme

ACHIEVEMENTS

The training of Malaria Medical Officers and ancillary personnel required, was provided in the plan, and the staff and facilities in the Malaria Institute of India were suitably expanded to meet this obligation Seventy five medical officers, six entomologists, 402 malaria inspectors, 14 engineers and 21 laboratory technicians have been trained from 1953 onwards at the Malaria Institute of India The latter is fully equipped to meet all the future training requirements of the personnel

To ensure uniformity of methods of control, assessment and accounting it was quickly realized that an operational guide was necessary This was prepared with due regard to the divergent conditions of endemicity, vectorial behaviour, population density, transmission period, communications and a host of other factors The document was deliberately called a ' Guide ' with the full knowledge that modifications would be necessary from time to time and place to place, to avoid harmful regimentation and provide full scope for individual initiative A second edition is already in the press

A detailed assessment of results is being done but the over all picture reveals progress The results, however, are not, and could not in their nature be expected to be uniform everywhere The quality and extent of control established with the inauguration of the National Malaria Control Programme has varied from State to State, being more intensive in the State [illegible]here malaria control operations had been well established prior to the nationa [illegible] less in the States where an organization had to [illegible] of the national plan A few States which had a good nucleus of malaria organization prior to the plan, have, however, not advanced to the degree and extent possible during the plan One among several reasons for this state of affairs appears to be a conflict in ideology and policies pursued by State Governments with reference to participation on voluntary basis of local people in developmental

plans in general Such voluntary participation in a malaria control programme has some obvious limitations

To achieve successful control in the entire country (or even a State) it is essential to spray all the houses in malarious areas for the requisite number of times within as short a period as possible The time interval between sprayings as well as the spraying periods are governed to a great extent, among other factors, by the periods of the year when malaria transmission actually occurs Experience has shown that neither of the above conditions can be effectively satisfied by utilizing voluntary labour which is not amenable to any kind of control

At the time of inception of the plan, there was no agency to manufacture standard spraying equipment in the country and all such equipment had, therefore to be imported In pursuance of a general policy local industry was stimulated to interest themselves in the manufacture of this equipment Full use was made of a specialist in the line, made available to the Institute by The Rockefeller Foundation to draw up a set of standard specifications based on the World Health Organization general specifications for sprayers, to suit local conditions The industry in the country has in the course of two years been able to produce standard equipment in sufficient number to avoid the necessity of importing this item altogether Besides, the easy availability of much needed spares has helped considerably in the smooth working of the programme

The production of insecticides locally during the plan period to make the country as nearly self sufficient as possible, by mobilizing both public and private sectors in the country, has progressed satisfactorily One D D T plant established in Delhi as a joint project by U N I C E F /W H O /Government of India has gone into production with an annual capacity of 700 tons and a second plant is proposed to be set up in the south with a capacity of 1,400 tons Steps have already been taken to double the capacity of the Delhi plant The private sector is producing B H C and it is expected that an equivalent of nearly 1,500 tons of D D T would be available

ANALYSIS OF RESULTS

The data received from the units in the monthly reports for the year 1953 1954 and 1954 1955 are under compilation and analysis Appendices I, II and III give (1) the population protected and D D T consumed, (2) the malaria indices, and (3) the morbidity figures

Appendix I is prepared on the basis of the largest number of houses sprayed in any one round of spraying during the transmission period and assuming the number of people per house as five The recommended dosage of D D T application is 200 mg per square foot in two applications of 100 mg each On the basis of the ass

be possible to pr

number of person

square surface of

not given a 200 mg dosage during the transmission season each year and/or if the number of persons per house is more or less than five per house as assumed It would, therefore, be necessary to make allowances for these variations when

interpreting the data presented in the table It would be seen that against a minimum of 3 8 persons protected per lb in Coorg, the maximum is 21 9 in Manipur in 1953 54 and corresponding figures for 1954 55 are 3 4 and 13 3 in Coorg and Manipur respectively

Appendix II indicates a general trend towards lowering of the malariometric indices in most of the States There are, however, a few States like Madhya Bharat, Tripura and Uttar Pradesh, where there is a reverse trend There is also a suggestion that some units in the States of Bombay, Mysore, and Coorg have reached the end point of malaria transmission

Appendix III presents comparative morbidity rates As indicated therein the difference in the number of malaria cases reported from the dispensaries in the unit areas for the two years is multiplied by ten to arrive at the total reduction in the number of malaria cases in the areas controlled in each State This estimate is based on the data presented by Sinton (1939)

It will be seen that there has been a fall of nearly 19 4 million malaria cases in 1954 1955 as compared to 1953 1954 It would appear that on the basis of three days sickness per case and a daily wage of Rs 2/ the amount of money saved would be nearly 11 64 crores of rupees very nearly the sum expected to be spent on the programme for the three year period

The data presented in Appendices II and III indicate only general trends Statistical analysis will be attempted later when complete reports have been received and compiled

COSTS

		1953–54 Rs	1954–55 Rs	1955–56 Rs
1	Expenditure by the Centre on equipment and material for the various units customs duty and expansion of the Malaria Institute of India	2 12 60 592	3 01 49 113	3 09 48 000*
2	Expenditure by the States	1 13 48 147	1 24 68 36	1 99 01 000 (budget)
	Total	3 26 08 739	4 26 17 475	5 08 49 000
		Total Rs 1 260 75 lakhs		

*Revised budget as anticipated

APPRAISAL OF THE SITUATION

The appraisal of the progress of the plan has necessarily to be against the backgrour ... The ... orking plan has ... or execution ... ted above, have been encountered and most of them have been surmounted It may now be appropriate to review the original objectives, targets and organization

particularly for assessment of results and future policy in respect of some of the States not coming up to expected standard

At the time when the N M C P was planned the factor of anopheline vectors developing resistance to insecticides had not assumed the importance it has within the last year or two Insect resistance to insecticide was certainly known but observations at that time appeared to indicate that the danger of resistance in anophelines was not so imminent as in the case of other insects which had a lower degree of natural susceptibility to insecticides But recent studies indicate that the danger is real The time taken by anophelines to develop resistance requires to be determined It would probably vary from species to species and a number of factors like dosage of insecticide and its deterioration etc will affect it In the circumstances if malaria is ' controlled within the time (actually eradicated [illegible] usly then and then [illegible] thus possibly avoid [illegible] in use Thus it is seen that the time factor has assumed considerable importance Once the resistance phenomenon is allowed to develop, the problem of rural malaria control with insecticides synthesised with chlorine, may become impracticable It is because of this factor that we have to re examine our original objectives and targets and modify them where necessary to suit present day concepts

The [illegible] o provide protection from [illegible] The scope of the plan [illegible] out 750 lakh (75 million) [illegible] 1955 In selecting this population out of the 200 million preference was to be given to those living in hyperendemic areas the potential food growing areas and for those living in community project areas within them The concept of eradication will involve the inclusion in the programme of all the areas even those of very low endemicity, and the States which have left out areas with spleen rates less than ten per cent in the original planning will have to reconsider their requirements

As [illegible] hase was limited to three ye[illegible] the experience elsewhere [illegible] sary to extend it by an additional period of two years so as to continue the full control operations for a period of at least five years The point to consider now would appear to be whether this additional period of two years followed by the necessary maintenance period would be sufficient to achieve malaria eradication? If eradication is to be the goal then ensurement of its achievement everywhere or at least in large contiguous areas, is of paramount importance This will require a very careful and continuous vigilance during the maintenance period after the end point is reached and will largely depend on the calibre and application of the vigilance staff in the units

The indices to determine the achievement of eradication have necessarily to be more sensitive than the ones we adopt at present to assess malaria control They will in all probability consume infinitely more time and involve greater expenditure in being determined One important essential factor in this connection will be a thorough search for every new case of malaria On this will depend the rest of the epidemiological verification investigation and measures to

eradicate the focus It will require intensive study to evolve quickly a suitable organization for spotting new cases and their microscopical verification

It has been indicated that each unit of the National Malaria Control Programme was designed to afford protection to one million population This has been found to be feasible only under certain conditions of population density, communications, etc There are, however, areas where population is scarce and communications scanty, in which circumstances the units are unable to cover much more than nearly half a million It may, therefore, be a more accurate overall estimate to place the target at 800,000 per unit on an average

The main emphasis of the National Malaria Control Programme was on malaria control in the rural areas With large rural areas under control and the conception of eradication having come in the fore-front, the problem of urban malaria has taken on a new urgency In the light of experience and repeated demonstration in this country and elsewhere, urban malaria control should, if feasible, be based largely on permanent engineering measures Such measures are not only more economical than the measures suited to control malaria in the rural areas but also take care of general mosquito nuisance Where there are other mosquito borne diseases, indeed, the permanent engineering measures are the ones of choice in their prevention, the second choice being given to recurrent anti-larval measures To the administrators and the public, the National Malaria Control Programme would appear to have come to mean the spraying of D D T

SUPERVISION

It has been pointed out that the pace at which control has been established has been greater in some States than in others It has also been indicated that such progress has not been uniform even in some of the States that had considerable experience and staff for malaria control prior to the advent of the plan In the States where there was little or no organization to control malaria prior to the plan, perhaps it was to be expected that the
the above, it would appear necessary now to
for greater supervision where necessary In
centres and utilizing the highly trained and experienced personnel, both at the Centre and the States, to staff such centres, seems essential to achieve the objectives in full during the second Five Year Plan

RESEARCH

It has been said that a unique contribution to science by America lies in making research a career and a normal avocation The realization that research is not something that is mystic, and should be pursued in exclusive laboratories by only a few who are removed from conditions in the field, does not yet seem to have pervaded this country, at least not widely enough among practical malariologists The problems to be solved are many, it is the field malariologist that comes across

the problem at first hand It is he that most requires a solution to each problem ientific lines Many of the problems of by work in the field and would be

A number of research projects covering the different aspects of the epidemiology and control are in progress The vectors of malaria in some areas like Tripura, Manipur, Vindhya Pradesh, Madhya Bharat, have been incriminated The insecticidal properties of the newer synthetic insecticides and the best material as also the most economical dosages of application, are under continuous study The normal susceptibility to D D T of the different malaria vector species and their present status after different periods of exposure to D D T, are currently under detailed investigation A technique for working with lower pressures in the spraying equipment has been developed

Perhaps the single most important problem of the day is insect resistance to insecticide The study of the problem requires planning, definition of objectives and priorities—a tremendous amount of work It requires no prophet to say that postponement of this phase of activity will be fatal to the cause of malaria control trained in ly to tackle are to be exploited before it is too late

PUBLICITY

It is a sad reflection that the progress of health activities in the country, not to mention the National Malaria Control Programme in particular, did not receive adequate publicity in the feature articles commemorating eighth year of freedom The reason for this must be sought Is it because that the National Malaria Control Programme is not sufficiently known to the people and the administrators? And yet in other contexts it has been stated times out of number that the National Malaria Control Programme is one of the very few health programmes under the National Plan that has made good progress and one of the very few projects in the entire plan whose benefits have been within the reach of an average householder The results achieved by the National Malaria Control Programme thus far are concrete and not imaginary or theoretical It would appear that the people and the administrators have not yet felt the tremendous activity with regard to prevention of malaria that is in progress in the country on a scale unprecedented anywhere in the world The necessity to get the people and the administrators to feel the progress and take a live interest, seems only obvious Publicity like everything else has to be planned and organized to be effective

PUBLIC PARTICIPATION

It is a sufficiently recognized principle that success in any large undertaking tivity The more active the public lertaking This principle has been at then is the practical feasibility of

publıc partıcıpatıon ın the Natıonal Malarıa Control Programme? It would appear to lıe ın the field of actıve cooperatıon wıth the dutıes of those who are traıned employed and paıd to carry out certaın functıons for protectıng the publ c from malarıa Such cooperatıon can only be obtaıned by educatıon of the people ın the ratıonale of the actıvıtıes

A technıque to carry the people all the way wıth the progress ıs to organ ze malarıa committees comprısıng representatıve members who wıll from tıme to tıme meet to take stock of the sıtuatıon progress dıfficultıes and obstacles and take steps to overcome them Such commıttees formed at all levels lıke the panchayat

Appendix I

Number of houses sprayed populatıon protected and the number protected per lb of D D T

S a e	19ɔ3–54				19ɔ4–55			
	Number of houses sprayed at least once	D D T con sumed (lbs)	Popu at on protected	Number of people protected per lb of D D T	Number of houses sprayed at least once	D D T con sumed (lbs)	Populat on protected	Numbe of people protected pe lb of D D T
Ajmer	4 481	38 8°6	°1° 405	5 4	67 080	6 610	33ɔ 400	5 1
Bhopal	88 574	°1 867 5	44° 870	°0 °	183 074	103 065	915 3 0	8 8
B har	°ɔ5 °10	87 049	1 °76 050	14 6	1 592 587	77 89	96 93ɔ	10 °
Bombay	3 °ɔ 999	1 638 660	16 264 995	9 9	3 486 399	1 676 54°	17 431 995	10 3
Coorg	39 479	51 4°8	197 395	3 8	38 801	57 015	194 005	3 4
Delh } Urban	63 3ɔ4	38 75°	316 770	8 1	10ɔ 657	53 3	ɔ18 °8ɔ	9 9
Delh } Rural	ɔ6 1°0	73 118	°50 600	3 8	0 673	99 071	353 36ɔ	3 5
H machal Pradesh	31 417	19 899	157 085	7 8	160 507	79 133	80° 535	5 0
Kutch	43 3°8	4 341	°16 640	8 9	69 387	34 0°	346 935	10 1
Madhya Bharat	°35 738	196 077	1 178 690	6 0	°73 446	°83 364	1 367 °30	4 8
Madhya Pradesh	1 487 74ɔ	451 8°1	7 438 7°5	16 4	1 558 9°°	683 65ɔ	7 794 810	11 4
Man pur	3 461	790	17 305	°1 9	66 50	°4 950	33 510	13 3
Mysore	687 43	367 096	3 437 160	9 3	63ɔ 6 9	60° 375	3 178 140	5 °
O ıssa	310 967	°03 895	1 534 835	7 6	1 05° °7	461 313	5 61 360	11 4
Punjab	°14 074	°08 34°	1 070 370	5 1	544 34°	610 307	° 7 1 710	4 4
P E P S U	159 157	77 958	79ɔ 78ɔ	10 °	409 956	°ɔ6 99°	2 049 780	9
Tr pura	°7 4°8	7 398	137 140	18 5	1 0 877	49 923	604 385	1° 1
Uttar Pradesh	15ɔ 584	48 413	777 9°0	16 0	296 7°4	°39 793	1 915 8ɔɔ	7 9
West Bengal	° 718 430	1 118 167	13 59° 150	1° 1	3 181 989	1 481 459	15 909 945	10 7

APPENDIX II.

Spleen rate, parasite rate and infant parasite rate in different States in India

State	1953–54			1954–55		
	Spleen rate (per cent)	Parasite rate (per cent)	Infant parasite rate (per cent)	Spleen rate (per cent)	Parasite rate (per cent)	Infant parasite rate (per cent)
Andhra	24 4/27 5	3 3/7 2	1 0/7 3	19 9/29 6	7 4/9 7	5 6/7 9
Bihar	11 9/59 6	9 5/16 8		11 2/39 6	0/21 3	0 0/13 3
Bombay	0 0/20 7	0 0/9 7	0 0/8 8	0 0/14 9	0 0/10 0	0 0/13 [illegible]
Coorg	0 02	0	0	0 02	0	0
Delhi Urban	0 18	0	0	0 06	0	0
Delhi Rural	1 30	0 1	0	0 80	0	0
Hyderabad	3 9/21 0	0 6/30 6	0	4 0/8 5	0 6/7 2	0 1 4
Kutch	6 4	13 4		4 1	5 8	
Madhya Bharat	7 8/26 6	14 7/23 0		14 5/25 6	9 9/15 7	
Madhya Pradesh	6 6/64 9		0/28 7	6 4/44 9	0/32 4	0/17 8
Manipur	23 2	1 5		17 7	1 0	0 8
Mysore	0/12 2	0/15 0	0/5 1	1 2/13 4	0 5/15 9	0/0 3
Orissa	29 9/41 5	1 6/1 9	3 8/33 3	24 7/27 3	0 3/1 7	0
Punjab	7/14 8		0/0 6	3 3/9 0	0/17 3	0/0 8
PEPSU	7 5/7 6	0 2/2 1	0	0 5/2 5	0	0
Saurashtra	22 1	0 6	0	11 1	0 5	0 9
Travancore Cochin	19 2	7 1	0	10 6	1 4	0
Tripura	55 8	17 1	14 2	61 1	21 6	12 5
Uttar Pradesh	5/24 9	0 6/15 5	0/14 2	11 4/28 3	1 5/10 1	0/11 4
Vindhya Pradesh	18 7/27 8			7 9/16 4		
West Bengal	5 3/64 1			2 7/53 0		

Note.—For purposes of conciseness, the spleen parasite and infant parasite rates are presented as ranges in each State The numerator in each instance represents the lowest rate and the denominator the highest amongst the different units in operation in each State

public participation in the National Malaria Control Programme? It would appear to lie in the field of active cooperation with the duties of those who are trained employed and paid to carry out certain functions for protecting the public from malaria Such cooperation can only be obtained by education of the people in the rationale of the activities

A technique to carry the people all the way with the progress is to organize malaria committees comprising representative members who will from time to time meet to take stock of the situation progress difficulties and obstacles and take steps to overcome them Such committees formed at all levels like the panchayat municipal district, State regional and national levels would help to keep the plan alive and bring home to the people the full realization of the possibilities of a nation free from such a crippling disease as malaria

APPENDIX I

Number of houses sprayed population protected and the number protected per lb of D D T

State	1953 54				1954–5			
	Number of houses sprayed at least once	D D T con sumed (lbs)	Popu at on protec ed	Number of people protected per lb of D D T	Number of houses sprayed at least once	D D T con sumed (lbs)	Populat on protected	Numbe of people pro ec ed per lb of D D T
Ajmer	4° 481	38 8 6	°1° 405	5 4	67 080	6ɔ 610	335 400	5 1
Bhopal	88 74	°1 867 5	44° 870	°0 °	183 074	103 065	915 370	8 8
B har	°55 °10	87 049	1 °76 050	14 6	1 59° 587	77 89°	7 96° 935	10 °
Bombay	3 °ɔ 999	1 638 660	16 °64 995	9 9	3 486 399	1 676 54°	17 431 995	10 3
Coorg	39 479	51 4°8	197 395	3 8	38 801	57 01ɔ	194 005	3 4
Delh } Urban	63 354	38 75°	316 770	8 1	105 657	ɔ3 3°	518 °8ɔ	9 9
Delh } Rural	56 1°0	73 118	°ɔ0 600	3 8	70 673	99 071	353 36ɔ	3 5
H machal Pradesh	31 417	19 899	157 085	7 8	160 507	79 133	80° 53	5 0
Kutch	43 3 8	°4 341	°16 640	8 9	69 387	34 0°°	346 935	10 1
Madhya Bharat	°35 738	196 077	1 178 690	6 0	°73 44(	°83 364	1 367 °30	4 8
Madhya Pradesh	1 487 45	4 1 8°1	7 438 7°ɔ	16 4	1 5ɔ8 9 2	683 655	7 794 810	11 4
Man pur	3 461	790	17 305	°1 9	66 50°	°4 9 0	33° 510	13 3
Mysore	687 43°	367 096	3 437 160	9 3	63ɔ 6 9	6ɔ° 375	3 178 140	5 °
Or ssa	310 967	°03 89ɔ	1 534 835	7 6	1 (ɔ° 272	4(1 313	ɔ ° 1 360	11 4
Punjab	°14 074	208 34°	1 070 370	5 1	544 34°	610 307	° 7°1 710	4 4
P E P S U	159 157	77 958	795 78ɔ	10 2	409 9ɔ6	°ɔ6 99	° 049 780	7 9
Tr pura	27 4°8	7 398	137 140	18 5	1 0 877	49 9 3	604 38ɔ	1° 1
Uttar Pradesh	1ɔ5 584	48 413	777 9 0	16 0	296 7°4	°39 793	1 915 85ɔ	7 9
West Bengal	2 718 430	1 118 167	13 59° 150	12 1	3 181 989	1 481 459	15 909 945	10 7

APPENDIX II

Spleen rate, parasite rate and infant parasite rate in different States in India

State	1953–54			1954–55		
	Spleen rate (per cent)	Parasite rate (per cent)	Infant parasite rate (per cent)	Spleen rate (per cent)	Parasite rate (per cent)	Infant parasite rate (per cent)
Andhra	24.4/27.5	3.3/7.2	1.0/7.3	19.9/29.6	7.4/9.7	5.6/7.9
Bihar	11.9/59.6	9.5/16.8		11.2/39.6	0/21.3	0.0/11.3
Bombay	0.0/20.7	0.0/9.7	0.0/8.8	0.0/14.9	0.0/10.0	0.0/13
Coorg	0.02	0	0	0.02	0	0
Delhi — Urban	0.18	0	0	0.06	0	0
Delhi — Rural	1.30	0.1	0	0.80	0	0
Hyderabad	3.9/21.0	0.6/30.6	0	4.0/8.5	0.6/7.2	0/1.4
Kutch	6.4	13.4		4.1	5.8	
Madhya Bharat	7.8/26.6	14.7/23.0		14.5/25.6	9.9/15.7	
Madhya Pradesh	6.6/64.9		0/28.7	6.4/44.9	0/32.4	0/17.8
Manipur	23.2	1.5		17.7	1.0	0.8
Mysore	0/12.2	0/15.0	0/5.1	1.2/13.4	0.5/15.9	0/0.3
Orissa	29.9/41.5	1.6/1.9	3.8/33.3	24.7/27.3	0.3/1.7	0
Punjab	7/14.8		0/0.6	3.3/9.0	0/17.3	0/0.8
P.E.P.S.U.	7.5/7.6	0.2/2.1	0	0.5/2.6	0	0
Saurashtra	22.1	0.6	0	11.1	0.5	0.9
Travancore-Cochin	19.2	7.1	0	10.6	1.4	0
Tripura	55.8	17.1	14.2	61.1	21.6	12.6
Uttar Pradesh	5/24.9	0.6/15.5	0/14.2	11.4/28.3	1.5/10.1	0/11.4
Vindhya Pradesh	18.7/27.8			7.9/16.4		
West Bengal	5.3/64.1			2.7/53.0		

Note.—For purposes of conciseness, the spleen, parasite and infant parasite rates are presented as ranges in each State. The numerator in each instance represents the lowest rate and the denominator the highest amongst the different units in operation in each State.

public participation in the National Malaria Control Programme? It would appear to lie in the field of active cooperation with the duties of those who are trained employed and paid to carry out certain functions for protecting the public from malaria Such cooperation can only be obtained by education of the people in the rationale of the activities

to overcome them Such committees formed at all levels like the panchayat

Appendix I

Number of houses sprayed population protected and the number protected per lb of D D T

State	1953-54				1954-55			
	Number of house sprayed at least once	D D T consumed (lbs)	Population protected	Number of people protected per lb of D D T	Number of houses sprayed at least once	D D T consumed (lbs)	Population protected	Number of peop… protected per lb D D T
Ajmer	4 481	38 826	12 405	5 4	67 080	6 610	335 400	5 1
Bhopal	88 574	21 867 5	44 870	20 2	183 074	103 065	915 370	8 8
Bihar	255 210	87 049	1 276 050	14 6	1 592 587	77 892	7 962 935	10 2
Bombay	3 25 999	1 638 660	16 264 995	9 9	3 486 399	1 676 542	17 431 995	10 3
Coorg	*39 479*	*51 428*	*197 395*	*3 8*	*38 801*	*57 015*	*194 005*	*3 4*
Delhi — Urban	63 354	38 752	316 770	8 1	105 657	53 32	518 285	9 9
Delhi — Rural	56 120	73 118	250 600	3 8	70 673	99 071	353 365	3 5
Himachal Pradesh	31 417	19 899	157 085	7 8	160 07	79 133	802 535	5 0
Kutch	43 3 8	24 341	216 640	8 9	69 387	34 022	340 935	10 1
Madhya Bharat	235 738	196 077	1 178 690	6 0	273 446	283 364	1 367 230	4 8
Madhya Pradesh	1 487 745	4 1 821	7 438 7 5	16 4	1 558 922	683 655	7 94 810	11 4
Manipur	3 461	790	17 305	21 9	66 502	24 950	332 510	13 3
Mysore	687 432	367 096	3 437 160	9 3	635 6 9	602 375	3 178 140	5 2
Orissa	310 967	203 895	1 534 835	7 6	1 052 272	461 313	5 261 360	11 4
Punjab	214 074	208 342	1 070 370	5 1	544 342	610 30	2 721 710	4 4
P E P S U	159 157	77 958	795 785	10 2	409 956	256 99	2 049 780	7 9
Tripura	27 428	7 398	137 140	18 5	120 877	49 923	604 385	12 1
Uttar Pradesh	155 584	48 413	777 920	16 0	296 24	239 793	1 915 8 5	7 9
West Bengal	2 718 430	1 118 167	13 59 150	12 1	3 181 989	1 481 459	15 909 945	10 7

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APPENDIX III.

State-wise reduction in malaria cases from the year 1953-54 to 1954-55

	State	Malaria cases reported from hospitals and dispensaries			On the assumption that one out of 10 cases reported to a dispensary, the total figure of fall in cases arrived at by multiplying the figures in Col 4 by 10
		1953–54	1954–55	Reduction from 1953 54 to 1954-55	
	1	2	3	4	5
1	Bhopal	1,44,205	1,00,774	43,430	4,34,300
2	Bihar	11,07,819	7,59,410	3,48,409	34,84,090
3	Bombay	2,53,006	1,95,229	57,777	5,77,770
4	Coorg	3,439	3,210	229	2,290
5	Delhi	9,172	7,035	2,137	21,370
6	Himachal Pradesh	1,01,110	81,838	19,272	1,92,720
7	Hyderabad	1,04,776	56,740	48,036	4,80,360
8	Kutch	18,202	12,094	6,108	61,080
9	Madhya Bharat	1,10,638	90,782	19,856	1,98,560
10	Madhya Pradesh	5,88,716	3,32,678	2,56,038	25,60,380
11	Madras	1,56,099	1,30,454	25,645	2,56,450
12	Manipur	65,260	55,813	9,447	94,470
13	Mysore	1,93,530	1,45,053	48,477	4,84,770
14	Orissa	14,234	7,192	7,042	70,420
15	P E P S U	1,03,330	61,505	41,825	4,18,250
16	Punjab	5,08,636	3,80,496	1,28,140	12,81,400
17	Saurashtra	47,597	33,381	14,216	1,42,160
18	Travancore Cochin	55,012	51,478	3,534	35,340
19	Tripura	1,27,339	90,877	36,462	3,64,620
20	Uttar Pradesh	6,03,644	5,55,882	47,762	4,77,620
21.	Vindhya Pradesh	94,314	64,741	29,563	2,95,630
22	West Bengal	16,18,924	8,76,955	7,41,969	74,19,690
	Total	60,29,001	40,93,627	19,35,374	1,93,53,740

Notes—The Director of Public Health, Andhra, has reported that 3,507 deaths occurred from malaria in 1954 as compared to 3,526 deaths in 1953

The Civil Surgeon, Ajmer, has stated that there was about 40 per cent fall in the number of malaria cases from 1953-54 to 1954-55

National Malaria Control Programme did not operate in the States of Assam, Jammu and Kashmir, Rajasthan and Coalfields during 1953-55.

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WORLD HEALTH ORGANIZATION (1954)

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MALARIA CONTROL IN THE PUNJAB (INDIA) WITH SPECIAL REFERENCE TO THE NATIONAL MALARIA CONTROL PROGRAMME

BY

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(*Malariologist, Malaria Organization, Punjab*)

(September [illegible] 195[illegible])

THE Punjab is a border State at the extreme north west corner of India After the partition of this Province in 1947, the State has been greatly truncated and instead of 27 districts, it consists at present only of 13 districts Except for the entire Kangra District and a small portion of Simla which are mountainous, the rest of the State is a great alluvial plain which stretches from the foot of the Himalayas to the Rajputana desert In other respects the country is featureless with the exception of mighty rivers which traverse the plains and are flooded almost every year after heavy monsoon rainfall The affected country-side is inundated extensively resulting in the loss of lives, property and outbreaks of malaria and other epidemic diseases

The soil of the Punjab is for the most part a fine silt deposited by the rivers whose action has virtually formed the land It is peculiarly impervious to water in most places and this, added to the level character of the country, results in large surface collections of water in the event of floods temporarily submerging extensive tracts of the State

Between the rivers of the Punjab are strips of country known as the '*Doabs*' These are situated on comparatively high level but they are not entirely safe from being adversely affected by heavy rainfall On the whole, the soil is very suitable for production of chief agricultural crops namely, cotton wheat, sugarcane, millets, gram rice, etc There is an extensive network of canals throughout the State which greatly help in the production of superior agricultural crops Other modes of irrigation are by wells in the plains and '*Kuhls*' in the hill tracts

According to the 1951 census, the total population of the Punjab has been estimated at 12 641,205 spread over a land area measuring 37,378 square miles The distribution of the population in 13 districts of the State is given below —

TABLE I.

Distribution of rural and urban population in the Punjab (India).

	District	Total population	Rural population	Urban population
1	Hissar	1,045,645	877 945	167 700
2	Rohtak	1,122,046	970,987	151 059
3	Gurgaon	967,664	827 511	140,153
4	Karnal	1,079,379	876,067	203,312
5	Ambala	943,734	695,784	247,950
6	Simla	46 150		46,150
7	Kangra	936,042	893,592	42,450
8	Hoshiarpur	1,091,986	986,962	105,024
9	Jullundur	1,055,600	761,202	294,398
10	Ludhiana	808,105	602,218	205,887
11	Ferozepore	*1,326,520*	*1,101,438*	*225,082*
12	Amritsar	1,367,040	958 533	408,507
13	Gurdaspur	851,294	688,034	163,260
	Total	12,641,205	10,240,273	2,400,932

As is usual in India, the rural population greatly exceeds the urban, being nearly eighty per cent of the total There are only three cities namely Amritsar, Jullundur and Ludhiana with a population exceeding 100,000. The housing conditions are more or less similar in the rural areas of the State The villages consist of solid mud built houses, lying compactly around the agricultural lands In the hill tracts, however, a village is conventional aggregate of small hamlets known as '*Tikas*' which are remotely scattered according to the situation of the agricultural land of the villagers The houses in the hills are usually smaller as compared to those in the plains.

The partition of the Punjab during August 1947 involved considerable exchange of populations between the East and West Punjabs—the latter having become part of Pakistan This exchange had a tremendous influence in introducing ... East Punjab ... rtain highly ... as populated predominantly by Muslims, had shown substantial lowering of malarial incidence after this mass exodus of infected Muslim population

The normal climate of the Punjab is characterized by extremes of cold and hot weather The cold weather gradually gives way to the hot weather at the end

of March, from which time it gets steadily hotter, and the relative humidity gets steadily less and less till the middle of June when great extremes of heat and dryness are normally experienced The monsoon breaks suddenly usually about the third week in June, with a consequent increase in the relative humidity and decrease in the maximum temperature The minimum temperature at night remains practically unchanged at about 80°F Periodical rain falls throughout the monsoon during July and August, gradually diminishing in September when the relative humidity again decreases Gradually the winter is ushered about the middle of November It has been observed (MacDonald and Majid 1931 that the monsoon is the sole apparent climate controlling factor in the spread of malaria, the amount of rainfall influencing the number of breeding places and the associated increase in humidity, which lasts just as long and no longer than the monsoon, making it possible for the anophelines to live a long time and consequently to be capable of transmitting malaria

INCIDENCE OF MALARIA

Nearly seven million out of a total population of nearly 12 6 million in the Punjab live in rural malarious tracts This disease is chiefly prevalent in the plains of the Punjab but in the hill tracts at an altitude varying from 2 000 to 4 000 feet above sea level, it has been reported to be very active Extensive areas in Kangra District are known to be highly malarious and in certain parts condition of malarial hyperendemicity have also been recorded

Malaria is endemic almost throughout the Punjab and manifests itself chiefly in the [illegible] Kangra hill tracts the malaria [illegible] comparatively more favourable [illegible]

In the plains of the Punjab, a very large number of endemic tracts exist which although may not exhibit epidemic conditions for years are in some ways so predisposed to them that on a certain minimum of rainfall they will become the seat of epidemic malaria Such tracts are located mostly near the rivers In addition, there are other areas which are not obviously riverain but nevertheless behave in the same way Such tracts usually receive much of the drainage from the district in which they are situated The foot hills throughout the State, more particularly near the Siwaliks in Hoshiarpur District develop epidemic conditions in this manner Such tracts not only easily become affected but exhibit a high degree of malarial intensity

As a measure of the endemicity of malaria the spleen and parasite indices have been studied during the course of malaria surveys conducted in different parts of the State in the recent years

Before the National Malaria Control Programme was introduced in the Punjab, the spleen rates amongst children under ten years of age in some of the important endemic areas of the State were as under —

District	Locality	Spleen rate (Per cent)
Kangra	Jowali	70.1
	Kulu	33.1
	Jowalamukhi	22.9
	Dera Gopipur	58.0
	Kangra	12.9
	Shahpur	24.3
	Nurpur	43.0
	Indaura	66.6
Gurdaspur	Behrampur	51.1
	Norat Jaimal Singh	28.1
	Siri Gobindpur	27.5
	Derababa Nanak	25.0
Amritsar	Patti	70.1
	Ram Das	27.9
	Taran Taran	24.5
	Ajnala	21.6
	Lopoke	29.8
	Majitha	21.6
	Chabal	24.2
	Tung Bala	58.0 } Suburban area
	Amritsar	40.5 }
Ferozepore	Guru Harsahai	89.3
	Zira	49.3
	Dharamkot	22.1
Ludhiana	Sidhwan Bet	47.6
	Machiwara	21.1
Hoshiarpur	Santokhgarh	31.1
	Gagret	34.0
	Amb	25.0
	Garh Shanker	22.9
	Hajipur	26.6

District	Locality	Spleen rate (per cent)
Karnal	Indri	38 0
	Thanesar	6 0
	Baj da	31
	Khojg pur	34 3
Rohtak	Gohana	[illegible]
	Juan	[illegible]
	Mundlana	3 8
Gurgaon	Dha j	[illegible]
	Sohna	[illegible]
	Punahana	[illegible]
	Hassanpur	[illegible]
Ambala	Panchkoola	[illegible]
	Chamkaur	[illegible]

It is evident that conditions of high endemicity and hyperendemicity evailed in the Punjab before the National Malaria Control Programme was troduced in 1953

Three species of malarial parasite, namely *P vivax P falciparum* and *malariæ* have been detected in the blood films examined from various parts of State The last named species is however very much restricted in its stribution

At intervals of years wide spread epidemics of malaria are liable to occur this State The disastrous epidemic of malaria which broke out during 1908 the Punjab, was of such a type where, in the space of three months it occasioned er 300 000 deaths amongst a population of approximately 20 000 000 Even fore this malarial epidemics of marked intensity had been experienced in 68 69 1877 78 1895 96 and in 1899 1900 (Gill 1928) Subsequent to the ar 1909 there have been several epidemics of malaria but the outstanding tbreaks were recorded in the years 1917 and 1923 1942 and 1950 Such idemics of malaria usually develop during years of excessive monsoon rainfall ociated with overflow of rivers following a series of years in which the rainfall s been in defect, and the greater the number of years which have elapsed since last epidemic year, the more likely is an epidemic to occur

As a result of the study of distribution of these malaria epidemics during the ig series of years it has been found that the districts of the Punjab vary in their bility to experience visitations of epidemic malaria For instance they do not cur in any part of the Himalayas although Kangra Valley is one of the most ensely malarious tracts The precise location of such wide spread epidemics of

malaria is more or less restricted to the low-lying plains which are liable to inundation

Amongst the chief factors which complicate malaria problem in the Punjab may be included (1) flooding of the rivers and the associated storm-water channels after excessive monsoon rainfall, (2) canal irrigation, (3) uncontrolled flow of storm water from hill sides into the adjoining low lying plains after heavy rains, (4) extensive swamps in low-lying areas which receive local drainage, as in Gurdaspur District and (5) the impounded water as a result of the construction of protective embankments in certain districts

At *least nine districts in the Punjab, namely, Gurdaspur, Amritsar,* Ludhiana, Jullundur, Hoshiarpur, Ferozepore, Karnal, Rohtak and Gurgaon are liable to inundations to a greater or lesser extent almost every year following excessive monsoon rainfall when the rivers Ravi, Beas, Sutlej and Yamuna are in spate Owing to the impervious nature of the soil, the flood water is retained for a sufficiently long period to create malariogenic conditions in such tracts

It is true that malaria has followed canal irrigation in the Punjab by raising the level of subsoil water and created swampy conditions in the adjoining areas Canal irrigation has become gravely prejudicial to health in areas where it has been improperly carried out Most of the districts in the Punjab, which are traversed by the great canal system, have become greatly menaced by malaria

In the hill tracts, the high incidence of malaria is usually associated with paddy cultivation which depends on the water supply from '*Kuhls*' arising from hill-streams

MALARIA FORECAST.

The Punjab perhaps claims a unique position inasmuch as it is only in this State that attempts have been made to develop and bring into administrative use a method for forecasting epidemics of malaria This method, as elaborated by Gill (1928) and Yacob and Satya Swaroop (1944), utilizes information pertaining to rainfall, enlargement of spleen amongst school children, economic conditions, and the variability of malarial incidence in individual localities recorded in previous years

This forecast, which is issued every year in the beginning of September, has proved of considerable value in past years in indicating areas in which more than ordinary prevalence of malaria has in fact subsequently occurred A malaria forecast of this type is certainly invaluable to a State which is every year exposed to malaria epidemics owing to the vagaries of monsoon rainfall

ANOPHELINE FAUNA

There are at least thirteen species of anopheline mosquitoes found in the East Punjab These are listed below —

A culicifacies	*A maculatus*
A fluviatilis	*A annularis*
A stephensi	*A pallidus*

A lindesayi
A pulcherrimus
A splendidus
A hyrcanus
A subpictus
A barbirostris
A gigas simlensis

Of these anophelines, *A culicifacies* is the accepted chief vector of malaria in the Punjab This is evident from the following results of dissections, carried out by different workers from time to time —

Observer	Species dissected	Number dissected	Gut infected	Gland infected
Perry (1910)	*A culicifacies*	100		
Gill and Singh (1917 20)	—do —	295		
Chowdhury (1930)	—do —	152	15	
Hicks and Majid (1931-36)	—do —	8 815	0	3
Mehta (1940-42)	—do —	455	1	6
Gill (1925)	*A stephensi*	155	3	3
Chowdhury (1930)	—do —	3		
Hicks and Majid (1931 36)	—do —	254		1
Mehta (1940)	*A stephensi*	42		
Chowdhury (1930)	*A fluviatilis*	24	2	
Hicks and Majid (1931 36)	—do —	381		1
Mehta (1940)	—do —	140		
Mehta (1940	*A maculatus*	21		
Mehta (1940)	*A pallidus*	103		
Chowdhury (1930)	—do —	7		
Chowdhury (1930)	*A splendidus*	26		
Hicks and Majid (1931 36)	—do —	98		
Mehta (1940)	—do —	21		
Stephens and Christophers (1902)	*A subpictus*	496		
Gill (1917)	—do —	102		
Hicks and Majid (1931-36)	—do —	159		
Hicks and Majid (1931 36)	*A annularis*	206		
Mehta (1940)	—do —	195		

From the above data it would be evident that *Anopheles stephensi* and *A fluviatilis* have also been incriminated in the carriage of malaria According to

Covell (1927), sporozoites were detected in the salivary glands of *A willmori* James by Adie (1911) in the Kangra Valley The precise role of this species in the transmission of malaria is being studied

The dissections of *A culicifacies* during different months of the year have indicated that the transmission of malaria is active chiefly from August to October In view of the fact that the transmission is so restricted, the measures aimed at the destruction of anopheline vectors have to be regulated accordingly

PREVIOUS HISTORY OF ANTIMALARIA WORK IN THE PUNJAB

The first serious attempt to study malaria problem in the Punjab relates to a report of a committee assembled to enquire into the salubrity of the area near Karnal watered by the Western Jamuna Canal (Dempster *et al*, 1847)

In the year 1908, the Punjab was visited by a regional malaria epidemic of marked severity in consequence of which an Imperial Malaria Conference was held at Simla during October 1909 and this led to the creation of the Punjab Malaria Bureau The functions of this institution were confined solely to the study of malaria in this Province Sometime later Christophers (1911) wrote a comprehensive memoir entitled *Malaria in the Punjab* ' which embodied a scientific exposition of the intricate malaria problems of the State These findings laid the foundation for further investigations on malaria (Perry, 1911, and Gill, 1914 1915 1917 1920 1921 1923 1924 1928)

During the subsequent reorganization of the Public Health Department Punjab, in 1923, the scope of the Malaria Bureau was enlarged so as to include the investigation and control of other epidemic and endemic diseases also This resulted in weakening the efforts towards the study of malaria In the year 1939 a field epidemiological unit was set up which was responsible for conducting malaria investigations and instituting antimalaria measures which consisted chiefly of the destruction of anophelines by pyrethrum sprays and administration of antimalaria drugs to the sick In addition limited antilarval measures were also applied

At the recommendations of the Bhore Committee (1946), a malaria organization was set up for the State with its headquarters at Lahore but before it could establish itself, the Punjab was faced in 1947 with partition based on political considerations

Prior to the year 1950, antimalaria measures were applied in the Punjab in a very restricted manner by the provision of a small antimalaria unit in each district and consequently feverish endeavours had to be made whenever serious outbreaks of malaria were reported Such recurring measures proved very expensive and helped in providing relief only for the time being

In the year 1950, the antimalaria policy was revised under the guidance of Lt-Colonel Jaswant Singh, Director, Malaria Institute of India Accordingly, the existing State Malaria Organization was expanded with its headquarters at Karnal [illegible] oratories where specialized [illegible] ides and other cognate p[illegible] demonstration

units were set up for combating rural malaria in Karnal and Gurgaon Districts and another malaria control project unit was detailed to demonstrate if malaria could be controlled in a badly affected urban tract like the city of Amritsar. During the period from the year 1950 to 1952, the number of demonstration teams was raised to five and these amply showed that under proper technical direction and control, a substantial lowering of malarial incidence could be achieved by the indoor application of insecticides such as D D T and B H C

NATIONAL MALARIA CONTROL PROGRAMME

In the year 1952, the total population protected against malaria by the State Malaria Organization was nearly four lacs (0 4 million) which involved an expenditure of nearly Rupees 2,61,000 This inadequacy of the protection afforded against malaria was realized by the Punjab Government early in 1953 when a bold and outstanding decision was taken to participate in the National Malaria Control Programme initiated by the Government of India under the Indo American Point IV Agreement During the year 1953 54, the Punjab Government earmarked a sum of Rs 7 47,700 towards this programme and the Government of India's contribution was nearly Rs 11,38,004 This assistance was in the shape of grants of D D T, antimalarials motor transports and essential spraying equipment provided through the Technical Cooperation Administration The expenditure on the operational costs was borne by the Punjab Government In this manner, four malaria control units were created for operation in areas worst affected by malaria in Gurgaon, Karnal, Rohtak Ambala, Ludhiana Ferozepore Gurdaspur, Amritsar and Kangra Districts

Intensive antimalaria operations consisted chiefly of indoor spraying of village houses with five per cent D D T watery suspension at a dosage of 100 mg per square foot twice during the malaria season These operations were commenced during July 1953, in nine out of the 13 districts of the State In the remaining districts routine antimalaria measures were applied by the normal anti epidemic staff on similar lines under the District Medical Officers of Health

Each malaria control unit consisted of one Medical Malaria Officer (Gazetted), eight Malaria Inspectors, 23 Sanitary Supervisors 120 Sanitary Beldars (field workers), five Motor drivers, five Cleaners and one Mechanic In addition, adequate personnel had been provided for the office of each unit at Gurgaon Karnal, Gurdaspur, and Ferozepore The mobility of the four Malaria Control Units was ensured by the provision of four trucks and one jeep for each unit

The programme of work was framed in advance taking into consideration the requirements of the areas to be served In this manner a total of 8,03 056 rooms in 2,526 villages were sprayed with D D T to afford protection against malaria In addition antimalaria drugs were administered by these units to 10,142 malaria cases By the application of these measures nearly 14,00,000 population was directly protected against malaria

These operations were also extended to deal with community projects of Faridabad, Sonepat, Nilokheri, Jagadhri and Batala, where 2,00,999 persons were

protected against malaria The community projects, as conceived by the Government of India, have been designed to promote the pre requisite for additional productivity, such as can cater for all the basic elements of rural life

Assessment of the first year's work under the National Malaria Control Programme in the Punjab indicated that although the target in regard to the total population to be protected could not be reached, still there had been a dramatic effect on the life of the people served by this project A reduction of 50,000 malaria cases was recorded in the recognized hospitals and dispensaries of areas in the State served by the National Malaria Control Programme In addition, there was a striking reduction in the spleen and parasite rates amongst the children Similarly, there was a conspicuous lowering of the population density of mosquitoes

The outstanding evil influence of malaria is directed towards the great loss of man power in industry and agriculture The economic gain to the Punjab as it affected the 'Grow More Food' campaign in the year 1953, has been estimated for Karnal and Ferozepore Districts It has been revealed that there had been an increase of 1,30,562 acres in the area cultivated in three tehsils namely, Karnal, Panipat and Kaithal during the period from July to December 1953 as compared to the preceding year Similarly, it has been estimated that there has been an increase of 11,327 acres in the area under paddy cultivation alone in three tehsils mentioned above which equals, by a modest official estimate of Rs 126 per acre, to a sum of Rs 14,27,202 This increase in the area under paddy cultivation has been reported only in the case of three tehsils in which intensive antimalaria measures have been carried out during 1953 On the other hand, in Thanesar Tehsil of Karnal District which could not be included in the National Malaria Control Programme there has been a marked reduction in the area under paddy cultivation Similarly there has been an increase in the area under paddy cultivation in Ferozepore District to the extent of 4,834 acres in 1953 as compared to the previous year which at a modest estimate equals Rs 6,03 084 Similar data is being collected from other districts also and it is expected that the net economic gain to the Punjab would definitely repay to a large extent the expenditure on malaria control programme (Rs 7,47,700) incurred by the Punjab Government during 1953

Encouraged by the results obtained, the Punjab Government extended their antimalaria programme so as to cover the entire State during the year 1954 For this purpose, seven malaria control units including the existing four units, were raised at an expenditure of nearly Rupees 10 8 lacs (1 08 million) Once again the Government of India, through the Technical Cooperation Mission, agreed to provide the required quantities of D D T, motor transports, essential spraying equipment, etc, at an approximate cost of nearly Rupees 8 5 lacs (0 85 million)

Seven malaria control units were accordingly raised, equipped and trained by June 1954, when intensive antimalaria operations were commenced throughout the State The disposition of these seven units, total population to be protected and areas to be covered are given below —

Units	Area to be covered (sq miles)	Population to be protected	
1 **Gurgaon Unit.**			
Gurgaon District	1,776 3	7 16,089	1 (9) (0
Rohtak District	590 0	2 83,911	
Karnal Unit.			
Rohtak District	826 6	3,7- 916	1 [illegible]
Karnal District	1,726 0	(,22 084	
Ambala Unit.			
Karnal District	542 0	1 88 (3)	1 [illegible] 00
Ambala District	960 0	4 4 481	
Hoshiarpur District	785 0	3 5 489	
4 **Jullundur Unit.**			
Ludhiana District	698 3	3 8 ,60	[illegible]
Jullundur District	380 1	3 01 00	
Hoshiarpur District	508 0	1 36	
Amritsar District	6) 9	4 31	
5 **Kangra Unit**			
Kangra District			
Gurdaspur District (Pathankot and Gurdaspur Tehsils)	3 0..0	4 ((	1
6 **Gurdaspur Unit**	712	1 3 [illegible]	
Gurdaspur District	560 0	3 24 (0	10 01 118
Amritsar District	971 0	6 058	
7 **Ferozepore Unit**			
Amritsar District	28 0	13 037	10,00,000
Ferozepore District	2,580 06	7,31 963	
Hissar District	1,306 0	2 55 000	
Total	18,070 26	70,01 118	

These units conducted malaria surveys in hitherto uninvestigated areas of State during April and May 1955 and intensive antimalaria operations were commenced during the following month The technique employed in regard to the functioning of the malaria control units was in conformity with the instructions contained in the '*Operations Guide*' issued by the Malaria Institute of India In

this manner 33,42,333 persons living in 5,868 villages were protected against malaria In this connection 20,24,400 rooms were sprayed with five per cent

twice during

In addition

Assessment of the antimalaria work carried out so far has revealed an unprecedented reduction in the number of malaria cases in the Punjab during the year 1954 as compared to the previous years This is evident from the data reproduced below —

Year	Number of malaria cases recorded in the hospitals and dispensaries of the State
1950	6,80,059
1951	5,11,775
1952	5,16,777
1953	5,08,636
1954	3,80,496

It will be observed that there has been a reduction of nearly 3,00,000 malaria cases

had not been

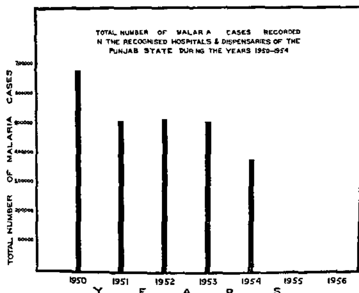
the State (Ch

Government dispensaries and hospitals Considering that a very large number of the affected population do not visit such centres of medical relief, it is expected that the total reduction in the number of malaria cases throughout the State during the whole year must be very great Similarly reductions in the (*i*) spleen rates of children (*ii*) parasite rates, and (*iii*) number of mosquitoes have been observed (Appendix I)

The transmission of malaria has been considerably reduced as indicated by pronounced lowering of infant parasite rates in all the areas served by the National Malaria Control Programme in the Punjab

From the foregoing account, it is evident that there has been a reduction of nearly 3,00,000 malaria cases during the year 1954 as compared to 1950 when residual insecticides had not been brought into use for malaria control on a very large scale throughout the State A case of malaria usually incapacitates a person for at least three to six days of his wage earning capacity At the lowest daily rate now provided by the various Governments, this involves a loss of Rs 12 per head on account of a single attack of malaria It is, therefore, evident that nearly Rs 36,00,000 were saved in terms of wage earning capacity of 3,00,000 persons protected from attacks of malaria during the second year of the National Malaria Control Programme in the Punjab State,

CHART I.



A substantial reduction in the number of fever deaths has also been reported in the Punjab during the year 1954 The relevant data are given below —

Year	Total number of fever deaths
1950	2,10,961
1951	1,58,871
1952	1,63,140
1953	1,84,858
1954	1,25,005

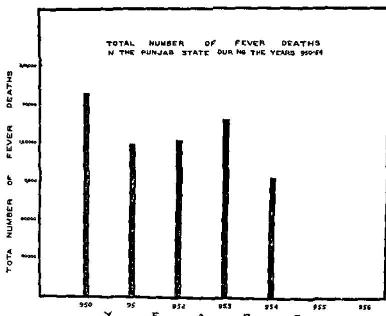
It will thus be observed that there had been a reduction of nearly 85,956 fever deaths in 1954 as compared to the year 1950 (Chart 2)

It is emphasized that apart from other advantages on account of the saving of 85 956 lives, there had been a net saving of Rs 42,97,800 which would have been spent on unprofitable funeral expenses

COLLATERAL BENEFITS

Amc
in the Pur
fleas, etc., which are usually abundan
yard-stick by which this could be measured except that there is considerable public appreciation in this field as manifested by the growing demand for D D T spray even in areas where malarial incidence is extremely low,

CHART 2



In the Punjab complete control against plague was effected in the year 1950 by the use of residual insecticides chiefly in the indoor rat harbourages This control has been effectively maintained up till now chiefly by indoor D D T spraying which has been carried out under the National Malaria Control Programme

The available data also indicate that there has been substantial reduction in the number of total deaths due to diarrhœa and dysentery in Amritsar District since the year 1951 when indoor spraying with D D T and B H C was carried out on a large scale for protecting the population against malaria The relevant data are reproduced below —

Year	Total deaths due to diarrhœa and dysentery	
1942	973	
1943	933	
1944	915	
1945	647	
1946	871	
1947	1 141	
1948	714	
1949	619	
1950	806	
1951	489	Mass indoor spraying with residual insecticides
1952	441	
1953	453	

CONCLUSIONS AND SUMMARY

Encouraging results have been achieved during the first two years of the working of the National Malaria Control Programme in the Punjab State

Besides the lowering of malarial incidence there has been considerable saving of human lives It has also been possible to improve the economic condition of the people by antimalaria operations A healthy and productive population is the basis of national economic progress which malaria definitely inhibits The National Malaria Control Programme was introduced at a very critical stage in the political life of the Punjab State which had been badly hit by partition during the year 1947 The alleviation of human suffering by intensive antimalaria operations has to a very large extent been responsible for the upgrading of the economic status of the people

Judging from the success attained and the progress maintained so far it is expected that the incidence of malaria would be driven to a very low point during the next few years as a result of the National Malaria Control Programme Having stopped malaria transmission, efforts will be concentrated on strategic control in order that malaria may not reappear

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Appendix I.

Spleen rates amongst children in the Punjab before the National Malaria Control Programme and in November, 1954.

District	Locality	Spleen rate before N M C P (per cent)	Spleen rate in November, 1954 (per cent)
Kangra	Nurpur	43 0	5 6
	Shahpur	24 3	16 2
	Jowali	70 1	16 8
	Dera Gopipur	58 0	5 9
	Jowalamukhi	22 9	11 4
	Kulu	33 1	12 0
	Indaura	66 6	14 8
Gurdaspur	Narot Jaimal Singh	28 1	10 8
	Behrampur	51 1	1 0
	Dera Baba Nanak	25 0	2 5
	Siri Gobindpur	27 5	4 8
Amritsar	Patti	70 1	1 3
	Ram Das	27 9	2 9
	Taran Taran	24 5	7 5
	Ajnala	21 6	4 1
	Lopoke	29 8	18 1
	Majitha	21 6	2 9
	Chabal	24 2	3 3
	Amritsar (suburban)	40 5	5 3
Ferozepore	Guru Har Sahai	89 3	3 0
	Zira	49 3	14 2
	Dharamkot	22 1	5 2
Ludhiana	Sidhwan Bet	47 6	2 0
	Machiwara	21 1	7 1
Hoshiarpur	Santokh Garh	31 1	5 3
	Garh Shanker	22 9	4 6
	Hajipur	26 0	21 3
Karnal	Indri	38 0	4 3
	Thanesar	26 9	1 9
	Khojgipur	34 3	4 3
Rohtak	Gohana	23 8	4 6
	Juan	22 9	0 0
Gurgaon	Dhauj	52 8	12 9
	Sohna	35 3	6 4
	Hassanpur	45 2	13 7
	Punahana	59 2	9 4

inert material such as road dust (Barber, 1941*b*) The use of this mixture beca standard procedure and remained so until 1936 when Barber suggested modification—paris green diluted with oil (kerosene) in the presence of egg albur (Barber, 1941*c*), instead of road dust When D D T came into prominer it was used in solution with oil (naphtha) to improve the quality of the larvi (Russell *et al*, 1946) These, then, were some of the popular materials develo to control mosquito larvæ To distribute these materials, hand equipment of type or another was used

Pyrethrins, the toxicant elements in pyrethrum, were first used to dest adult mosquitoes late in the 1930's (Thornton, 1935) The toxicant was dissolved in kerosene and applied as a space spray The efficiency of the method was proved in India early in the following decade (Russell *et al*, 1943), and for a time this spray solution was widely used in spite of its high cost and its lack of residual killing properties

Pyrethrum space sprays do not compare, though, in overall residual effectiveness, with the newer toxicants represented by chlorinated hydrocarbons commonly referred to as the D D T group These sprays, properly applied to the resting places of adult mosquitoes, have brought about radically beneficial results in malaria control throughout the world

Any agent for mosquito control must be applied Whether the agent is oil, paris green, pyrethrum, or D D T, it must be distributed by some type of equipment to the resting place of the larvæ or the adult For a long time the development of such equipment was left mostly to chance Certain types for instance knapsack sprayers, were taken over from other fields with little attempt to modify them in relation to the new problem In fact, no active effort was made to develop hand equipment for malaria control until pyrethrum came into use as a space spray Since
The movement has gai
Health Organization
standardization of hand operated equipment has rapidly advanced to the po where spray equipment manufacturers everywhere actively seek the Committee's advice

In the early days of larviciding, when oil was first used, it was apparently applied with any tool at hand Sometimes the oil was poured directly on the water surface from a container, and spread only because of its repellency toward water No effort at economy was made, and no spreading agent was knowingly employed Sprinkling containers of the garden type were frequently used, perhaps the first equipment employed to dispense oil on water as a mosquito control measure Once malaria transmission had been linked to the mosquito knapsack sprayers such as those used in agriculture were taken over and used without modification Throughout practically the entire larviciding era, only slight improvement which could be directly attributed to malaria control influences was made in this apparatus Even today, wherever the knapsack sprayer is still used it remains the same heavy, cumbersome oiler No real attempt has ever been made to improve the quality of discharge from the nozzle tip in order to secure better spreading of the larvicide Actually, little thought was given during the early years to the improvement of larviciding by use of oil, today, because of

the efficiency of other control methods, so little larviciding is carried on that specialized equipment for this means of control is hardly considered necessary

The knapsack sprayer may be symbolic of all hand larviciding oil equipment It was pressed into service, performed a useful function without undergoing extensive alteration and has been almost entirely replaced by techniques better suited to the solution of the problem

When Barber and Hayne developed the technique of destroying *Anopheles* larvæ by spreading paris green on water surfaces, they recognized the need for using a very small quantity of paris green per unit of water surface Consequently a way to dilute paris green had to be devised, and it was necessary to find some inert material with which the toxicant could be mixed Ordinary road dust became the popular diluent

It was quite a task to prepare this diluent First the dust had to be collected, and in malarious areas it was not unusual to see gangs of men along a well travelled highway assiduously collecting road dust Then the dust had to be screened an efficient hand operated device was constructed for the purpose This device was probably one of the first pieces of equipment designed primarily for use in malaria control, another was the mixing drum for combining the dust with the toxicant Such equipment is now usually found only in museums featuring discarded control methods

After a proper larviciding mixture of paris green and dust had been prepared it still had to be distributed A common early method was to put the mixture in a bucket and throw it by hand onto the water surface Hand bellows to which a small hopper containing the mixture was attached, were also used A pipe carried the mixture from the hopper to the tip of the bellows, where ejection under low air pressure took place whenever the bellows was operated This outfit had advantages over hand distribution, but the low capacity of the hopper as well as other draw backs of a mechanical nature, weighed against great popularity of the apparatus

Probably the most popular equipment for the distribution of road dust was a type of knapsack duster held on the operator s back with straps It consisted of a hopper with a capacity of about one cubic foot of mixture and a bellows arrangement, activated by a hand lever, which pumped air under low pressure and fair volume into a small compartment of the duster This compartment was automatically refilled with dust Air pressure agitated the dust The dust air mixture escaped [illegible] is deposited on water in fairly uniform quanti[illegible] the apparatus were developed, the principle [illegible] unchanged Distributors of this type continued in use in diminishing numbers as long as the road dust paris green technique survived, or until about 1937 38

Beginning about 1930, demand slowly grew for improved equipment, particularly for hand operated dust distributors with rotary blowers As with the knapsack larviciding machine, these rotary blowers were borrowed from agriculture and were not efficiently designed The difficulties experienced in their use were many indeed Because most of them were badly assembled, they leaked dust through every seam In addition, little attention had been paid to "balance", with the result that prolonged use tired the operator excessively Air

passages were not streamlined, this resulted in low-grade dust distribution Gears and cranks were crudely made Air vents and accompanying fans were not constructed to render maximum air delivery with a minimum of effort One example of such equipment was a square box referred to by the makers as a venturi It was used as a mixing chamber for air and dust This box, in no sense a venturi, frequently became clogged and caused endless trouble Furthermore, as the operator walked forward to dust a water surface, he had to turn the crank counter clockwise, in order for the apparatus to function at all!

Considerable improvement was made in this type of distributor during the following six or eight years, until the rotary duster was no longer extensively used for malaria control Possibly due to the need for a better product for malaria operations twenty years ago, this machine is much more substantial and dependable today and is still extensively used in agriculture

A very important revolution in equipment was brought about after 1936 by the introduction of Barber's wet method of paris green distribution This method soon eliminated road dust as a diluent It was no longer necessary to collect, screen, and store vast quantities of dust, nor was it necessary to mix and distribute tons of powder Instead, an operator carried with him sufficient kerosene paris green mixture to last one day Water was always available to dilute the mixture to proper proportions

This system of larviciding required completely different equipment, a type best operated by developing air pressure in the mixture container The mixture was ejected through a primitive type of nozzle in the form of a spray which readily spread a thin film over the water surface The apparatus was the forerunner of the hand compression sprayer so extensively used in residual spray operations during recent years These original hand compression sprayers had mechanical and structural weaknesses, but they were the most efficient tools used for malaria control through the kerosene paris green control period

Other types of equipment were put into service during the late 1930's and early 1940's These were, in fact, the real pioneer years for designing equipment adapted to malaria control Most equipment proved inadequate for the proper distribution of insecticides, however, until about 1940 Since then equipment has been designed more and more to meet this specific problem

One type of equipment worthy of note for larvicide application was the automatic paris green distributor, a machine originally designed in the Philippines and later perfected in India, which distributed proper quantities of paris green continuously over irrigation canals (Knipe and Russell, 1942) Current in the canals activated the distributor, and the same current carried a charcoal paris green mixture downstream with it, doing a remarkably efficient job of larvæ destruction *en route* However, popularity of the apparatus waned when the kerosene paris green mixture became popular, even though the equipment could readily be adapted to distribute this material

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northern India in the late 1930's (Covell *et al*, 1938) Beginning in 1939, an

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these cheap sprayers were not well made, did not sufficiently atomize the spray, were small in size, and were inadequately designed In order to overcome these defects, certain modifications were made an adequate nozzle tip which assured good atomization was constructed

pattern) was evolved in Delhi It possessed all the qualities of good atomiser It was widely used in civil organizations and by the army in all contonments and in forward areas during war years

Many other models of sprayers were investigated and developed in this project in southern India One of these dispersed space sprays through the use of "dry ice"—
1942) This a
was the so-call
This unit, which weighed only 28 pounds and was entirely self-contained, was quite efficient Still another model tried successfully was the prepressurized unit—the prototype of the present day hand compression sprayer This was pressurized, through a Shrader valve, to 100 pounds per square inch from one of several different sources of air pressure (Knipe and Sitapathy, 1942) A modified Cobra sprayer unit carried the insecticide, which was ejected and atomized by air pressure stored in the hand compression sprayer tank

At this time the need for some sort of regulator to control pressure on the nozzle tip was recognized, and a lightweight commercial regulator was found which served the purpose

and Sitapathy, 1942) This regulator was the forerunner of the present-day pressure regulator now advocated for use in one form or another on practically all types of residual spray equipment, whether power driven or hand activated

popularity of pyrethrum quickly receded

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sprayers, used practically throughout the world, and the stirrup-pump sprayer, widely used in India but not to any extent in other countries

An excellent residue of toxicants may be applied with either type of sprayer Although the sprayers differ considerably in action, the same amount of insecticide is distributed since distribution is made through the same type of liquid discharge line by each type Features of this line which have undergone intensive investigation include the following a bayonet type of attachment (for the hand compression sprayer), a polyvinyl chloride (a plastic), lightweight, highly abrasive resistant hose, a cut off valve which does not leak, a sturdy lance, an automatic non drip valve in the nozzle, and a carefully designed stainless steel nozzle tip which accurately determines the desirable flat spray pattern as well as the rate and angle of discharge

Since the hand compression sprayer is the type universally used, it has been subject to the greatest improvement In contrast to its prototype, which was at best, a cheaply designed agricultural tool with many defects, the present day hand compression sprayer is a first class tool for residual spray application and meets practically every requirement demanded of it This equipment has long since surpassed its predecessor the agricultural sprayer, in quality Features include an all stainless steel tank construction, welded seams which ensure against leakage, an adequate filler hole which may be semiautomatic in action, a Shrader [illegible] fety features, plastic leak proof gaskets, a [illegible] the equipment, and a bayonet connection [illegible] line

These improvements have been made through the cooperation of individuals working on malaria control projects who have consulted with interested equipment manufacturers in several countries Much of the coordination of details in the programme of development has been carried on by the World Health Organization Committee previously mentioned This Committee meets from time to time to discuss equipment and to formulate specifications of a general nature which seem to lend themselves to acceptance on a world wide basis

Hand equipment used in the field of malaria control has indeed passed through an interesting period of development The early prototypes, borrowed from any available source, served a purpose They were not always suited to the problem, but successful modifications were usually made Then specialized models, such as the automatic paris green distributor, began to appear Later, types adaptable to pyrethrum distribution were developed and gradually improved with the result that when residual sprays appeared, operators in the malaria control field were fairly well acquainted with the types of equipment required Models have now been perfected to the point where a malaria officer knows he has dependable equipment with which to carry on his control programme In fact, spray equipment for malaria control is now of such excellence that technical features are being copied for use in other insect pest control programmes

The advances made thus far do not mean that the perfect apparatus has been designed Improvements will continue to be made Everyone would like to escape the drudgery of pumping or pressurizing, a problem that may be solved [illegible] er press re reg lator control mechan sms will be designed

tion

In other words, spray equipment, like most modern equipment, has gone through several periods of development and change Today's equipment is far superior to yesterday's The end is still not in sight.

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ON THE POSSIBILITY OF *A SUNDAICUS* ERADICATION IN INDIA

BY

V VENKAT RAO, F R E S, M R S H

(July 15 1955)

THAT it is possible to eradicate vector anophelines from particular areas under certain conditions, and thus to eliminate permanently all chances of malaria transmission there, has been amply borne out by recent work The eradication measures which have so far been carried out successfully may be broadly classified into three groups as follows —

(*a*) Measures dealing with imported vectors,

(*b*) Measures carried out in limited areas having natural barriers, and

(*c*) Measures where eradication is obtained, not by deliberate action, but rather unexpectedly as a bye product of indoor residual spraying with insecticides

The first concerted attempt at eradication, which falls in the first category mentioned above and which was attended with conspicuous success, was made in Brazil by Soper and Wilson (1943) against *A gambiæ* and the next attempt was also made against the same species by Shousha (1948) in Egypt with similar results These measures involved antilarval as well as anti adult operations, though it was recognized that the former constituted the primary means of attack with the latter only as supplemental measures wherever necessary In both cases, paris green was used against the larvæ and pyrethrum against the adults Soper and Wilson (1943), however, cautiously observed that their success was due to the fact that the vector was imported into Brazil less than ten years previously and did not yet gain a firm foothold in the country and that *A gambiæ*, having selective breeding habits, was more vulnerable to attack than other species which are capable of breeding in a large variety of waters They doubted whether eradication would ever be possible with autochthonous vector species

After the advent of D D T, when it became possible to contemplate the elimination of malaria on a global scale, eradication was tried in Cyprus and Sardinia, two small islands in the Mediterranean Sea Whereas complete success was obtained in Cyprus (Aziz, 1948), the vector of Sardinia has not yet been wholly

eradicated, though it exists in only very small numbers and malaria is brought completely under control (Logan, 1953) In these cases also, anti adult measures were supplemented by antilarval measures

On the other hand, eradication as a bye-product of indoor residual spraying with D D T has been observed by several workers in various parts of the world Gabaldon (1949) and Giglioli (1951) have reported the eradication of *A darlingi* from Venezuela and British Guiana, respectively Dowling (1951) and Hamon and Dufour (1952) have succeeded in eradicating *A funestus* from Mauritius and Reunion *A sacharovi* has been eliminated from certain parts of Italy (Missiroli, Mosna and Allessandrini, 1948) *A minimus*, a notorious vector of the Oriental Region, has been virtually eliminated from the sprayed areas of Thailand (Dy, 1954) It should, however, be noted that all these cases have been observed on the border-line areas of the geographical distribution of the species concerned (Gabaldon, 1953)

It, therefore, appears that eradication is possible where the vector is imported into a new region, where the area concerned is limited and bound by [illegible] be marginal

[illegible]

A sundaicus is a species of the Malayan sub region of zoological distribution and is not properly a member of the Indian anopheline fauna The only locality in India where it is known to exist with certainty for a long time is the Sunderbans in the deltaic tracts of the rivers Ganges and Brahmaputra (Christophers, 1933) where physical features and ecological conditions are similar to those in the Malayan region Howev [illegible] tion was extended up to [illegible] (Gravely, 1912) In 193 [illegible] Budge, only 16 miles from [illegible] it occupied practically th [illegible] lakes of Calcutta and even extended westward up to about 20 miles from that city Severe malaria outbreaks occurred in all these areas soon after they were invaded by *sundaicus*

Another area where *sundaicus* is known to exist is around the Chilka Lake in Orissa, though for how long it has been there cannot be definitely stated When Hunter (1872) toured the area extensively to prepare a comprehensive report on Orissa to the Government, there was no malaria around the Lake, though Puri Town towards the north and Ganjam Town towards the south of the Lake, were observed to be malarious However, after a lapse of 40 years, Fry (1912) found an intense degree of malaria infection in the same area, with child spleen rates indicating hyperendemic conditions along the Lake shore Sarathy (1932) observed similar conditions twenty years later, showing that there was little change in the situation during the intervening period Though the time of invasion of Puri is not certain, there is some evidence of when the invasion of Ganjam took place Ganjam is situated about five miles to the south of the Lake This was a flourishing port and the local headquarters of the East India Company, with a population of 35,000, till 1815, when a violent epidemic of malaria occurred The

town was then abandoned by the Company and soon became a ruined and insignificant place. If we assume, as perhaps we must, that the malaria in Puri and Ganjam found by Hunter (1872) was due to the presence of *sundaicus*, it was about the year 1815 that *sundaicus* first invaded this area (Senior White and Venkat Rao, 1946). Though the mosquito was present in these two isolated places, it did not extend into the Chilka Lake as long as the Lake had direct access to the sea and its water was too saline for the mosquito to thrive. The subsequent choking up of the outlet and the resultant freshening of the water and the abundant growth of fresh water flora there might, in later years, have facilitated the rapid extension of the mosquito into this area (Venkat Rao, 1949).

The next extension, which was directed southwards, appears to have taken place during or about the year 1930, when violent epidemic exacerbations were reported from Chatrapur Town (five miles south of Ganjam) and from a somewhat extensive area further down the coast known as the "Uddanam", including Naupada, a salt manufacturing centre. Both these areas were previously healthy, having been used as sea side health resorts for a number of years. While, as in the case of Puri (Panigrahi 1942), Chatrapur suffered only from periodical epidemic outbreaks, highly endemic conditions were soon established in the Uddanam area, which became notorious for what came to be known locally as "coastal malaria".

Curiously enough, the latest infiltration to occur was not directed southward along the coast as might have been expected but extended inland up to about twenty miles from the sea, though the worst affected localities were situated within ten miles of the coast. This happened during the years 1942 and 1943 (Senior White *et al*, 1947).

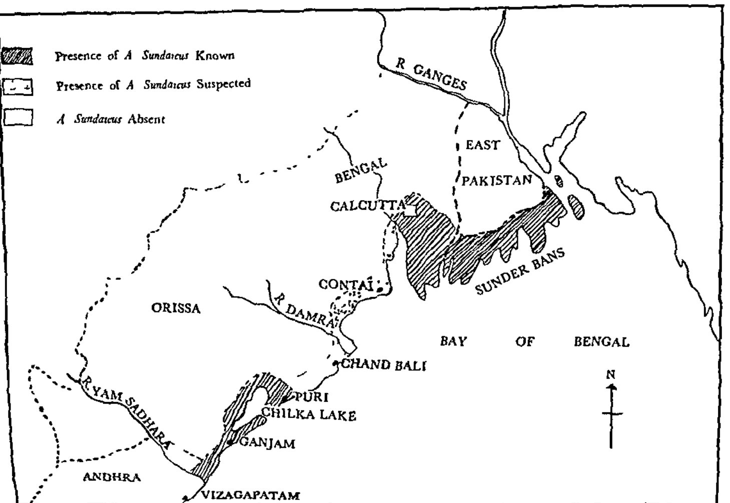
Thus, the areas where *sundaicus* is now known to be present are Lower Bengal, Chilka Lake area and the coastal tracts of Ganjam and North Vizagapatnam districts (Map 1).

The mechanism of extension of this mosquito into Lower Bengal has been described by some authors. After a careful investigation of the means of transport available in Bengal, Sen (1941), observed that, though railway trains were also partly involved, it was the small "country" boats plying the various localities between Sunderbans and Calcutta that were really responsible for the establishment of the mosquito in Calcutta, and that particularly active dispersal occurred during the years 1933 and 1934. This might possibly have been connected with the increased forest fellings followed by rice cultivation near Port Canning (Senior White, 1937).

The first invasion of Puri and Ganjam in the early years of the last century might have been facilitated likewise by small sea going vessels plying between Bengal and Orissa. At that time railways did not exist in India.

It is, however, obvious that the mere availability of railway and boat transport does not by itself result in the expansion of the mosquito into new areas. A number of railway trains run daily between the Chilka Lake and other *sundaicus* infested areas [illegible]

MAP 1.
North-East India



The invasion of Chatrapur Town, which is only five miles south of Ganjam, occurred over a hundred years after Ganjam was itself invaded, while the area immediately south of Chatrapur remained free from *sundaicus* for at least ten years more Probably, it is not availability of means of transport but a cataclysmic disturbance like a sudden and unprecedented increase in the population of the species that is responsible for bursts of colonization Deforestation and extended cultivation near Port Canning referred to above might have resulted in augmentation of breeding places and therefore, in the increase of *sundaicus* population in that area. During 1942, there was an immense increase in the prevalence of *sundaicus* in the Chilka area, pushing up the density in houses to over one hundred per man hour (Venkat Rao *et al*, 1942) As Senior White (1948) has observed, passive migration may extend the species into new areas but it is likely to die out there, as it did in the areas west of Calcutta

It is thus shown that, except in the Sunderbans, *sundaicus* is an imported mosquito everywhere else Except in the isolated localities of Puri and Ganjam where the mosquito appears to have been introduced over a hundred years ago, the importation into the other areas occurred in more recent times, the last burst occurring only about twelve years ago

Regarding the second postulate, *viz*, limitation by natural barriers, it is clear that *sundaicus* has a strong predilection for coastal conditions and does not exist far away from coastal and brackish water areas In Bengal, it has never been found more than six miles from tidal waters (Senior White and Venkat Rao, 1946) Throughout the Chilka area, if isolated collections in small numbers are excluded, the species does not exist beyond a maximum of five miles from the Lake Further south, including extreme cases, it has never been recorded from places over twenty miles from the Bay of Bengal It has now disappeared, either spontaneously or as a result of control measures almost entirely from this area

A sundaicus has not been recorded south of the River Vamsadhara Christophers (1933) referred to *sundaicus* (then known as *ludlowi*) as having been included in the list of Colombo mosquitoes by James in 1914 but it has not since been recorded there and is thought by Carter not to occur in Ceylon

Thus, the *sundaicus* infested area in the present West Bengal is only about 1,000 sq miles, while in Orissa and North Vizagapatam areas, the extent is approximately 1,500 sq miles

The 200-mile length of the coast between Puri and Calcutta has not been surveyed and whether *sundaicus* is present there either continuously or in isolated patches, is completely unknown The only reference to malaria prevalence in the area is made by Hunter (1872) who says that fever of low malarious type" is prevalent everywhere and specially so at the mouth of the River Damra, which is about as unhealthy as any found in Bengal and that the malaria season extends from August to October It is also known that the port of Chandbali is highly malarious The presence of *sundaicus* may be suspected in both the cases It, however, appears that continuous distribution of *sundaicus* all along the coast is not very probable as suitable estuarine conditions are seldom found without considerable separatory areas There are, at least, some known healthy spots on this coast like Contai and Digha The infested area, if there is any, is thus unlikely

to be more than a thousand square miles in extent, making a total of 3,500 square miles

If *sundaicus* has not extended further inland than it has already done, it is not because of natural barriers but because the mosquito is incapable of doing so owing to its evident need for an equable climate In fact, the only trait it still exhibits in common with its original home, Indonesia, is its association with the sea shore

For all practical purposes, therefore, *sundaicus* has a limited distribution and is subject to constitutionally imposed barriers against further expansion inland

As the presence of *A sundaicus* has been recorded only on the east coast of India between the Sunderbans and the mouth of the Vamsadhara River and nowhere else, either in India itself or in the countries west of India, it is definite that the area of its present prevalence is the westernmost limit of its area of distribution *A sundaicus* here is occupying an extremely narrow marginal zone

The situation is, however, complicated by the presence, at least in Orissa and North Vizagapatnam areas of two forms of *sundaicus*, one breeding in fresh waters and the other in saline waters According to epidemiological evidence, the fresh water form appears to be a potent vector of malaria, while the other form is at best a vector of secondary importance (Senior White *et al*, 1947)

Now, *sundaicus* has been recognized to be pre eminently a salt water breeder everywhere The only reference in the previous literature to fresh water *sundaicus* is made by Bonne Wepster and Swellengrebel (1953), who have stated that there was a fresh water form in Sumatra, that it was a potent vector there and that it was eliminated when its breeding places—fresh water fish ponds—were eradicated Thus, fresh water *sundaicus* appears to have existed in Sumatra and still exists in India, which are the eastern and western margins of the area of *sundaicus* distribution

The salt water breeding *sundaicus* has always been looked upon as a very effective carrier of malaria in the coastal regions of all countries wherever it occurs However, Taylor (1943) observed that, owing to the lack of direct correlation between the presence of this species and malaria on all occasions in Singapore it had been thought that *A sundaicus* of that island might consist of more than one species or variety and that more recent work indicated that this "supposition" was correct If, as is presumably the case, he referred to salt water breeders only, it appears that, even among them, there are forms which are vectors and others which are not Even in the Arakan region of Burma, Lalor (1912), Feegrade (1924) and Macan and Watson (quoted by Fox, 1949) dissected altogether 908 *specimens with negative results and therefore, prima facie, sundaicus* is not a vector there too No fresh water breeding has ever been recorded from this area

The available information indicates that, while there may be, among salt water breeders, some non vector forms, the fresh water forms are potent vectors wherever they exist Subsequent work carried out by Venkat Rao and [illegible] patnam area has shown that the two forms [illegible] to differences in the number and shape [illegible] what similar to those observed in the [illegible] Wepster and Swellengrebel, 1953)

It cannot perhaps be assumed that the two forms of *sundaicus* have always been present in this area, the fresh water form, which is located in recent years, should then have evolved out of the earlier salt water form Huxley (1942) has observed that a single species may separate gradually into two or more divergent lines transcending the limits of species distinction and that the separation into two mutually infertile or otherwise distinct groups may occur suddenly though the subsequent divergence may be gradual He goes on to state that ecological but spatially overlapping differentiation will promote divergence in general characters since more complete adaptation to two ecological niches will be advantageous to both species Probably, when *sundaicus* is faced with the problem of heavy overpopulation, it is capable of meeting the situation by separating, more or less suddenly, into two or more groups, each occupying a different ecological zone When they are thus separated, they may not merge again into one species through cross mating Though the variations in male genitalia mentioned above may not raise a mechanical barrier to copulation between the sexes of the two forms, there is an imponderable factor of a physiological nature operating against cross mating in such cases (Fennah, 1946) However, as both forms exhibit a marked preference to the ecoclimate of the sea coast and are present together within the same areas, and as both the forms have been found to be vectors in some area or other, this question, so far as eradication is concerned, may not require further discussion

Having shown that all the three conditions postulated for a successful eradication campaign are satisfied in a large measure in the case of *sundaicus*, the specific measures which should be undertaken for the purpose, shall now be considered :

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if one has to carry out indoor residual spraying continuously over a number of

(1954) has reported that *sundaicus* in the Djakarta area of Indonesia has developed chemico-resistance against D D T, though not yet to dieldrin, after a few years' spraying indoors Therefore, as in all other cases where eradication has been purposely aimed at, antilarval measures should constitute the primary means of attack, though indoor spraying should also be pursued simultaneously

ricefields is minimal, being restricted to the mouths of rivers and the narrow belt of ricefields along the margins of large bodies of saline water like the Chilka Lake The association of *sundaicus* with aquatic vegetation is very striking and the species will apparently breed in the presence of many different types of vegetation

While dealing mainly with salt waters, Covell and Singh (1942) have pointed out that it is only when the vegetation comes above the water surface and begins to putrefy that the larvæ of this species are found This suggests that water

polluted by rotting vegetation favours the breeding This is in accordance with the observations of Iyengar (1931) that, besides salinity, organic pollution of the breeding place is a cardinal condition of *sundaicus* breeding Can this be the reason for the poor vectorial status of the salt water form, at least in the Chilka area? The critical experiments of Russell and Mohan (1939, 1940) have shown this to be a wrong premise but Muirhead Thomson (1951) observed that in these experiments the pollution was of animal origin and that it still remained to be seen if gross pollution of the larval environment with vegetable organic matter—*a much more widespread phenomenon in nature—would have any effect on the* susceptibility of infection of the resulting adults However, Venkat Rao and Ramakrishna (1947*a*) have shown that, breeding of the fresh water form occurs in waters which are clear and good enough for the people to use for drinking purposes and that, when the vegetation is removed, the water becomes turbid and polluted and the green alga, *Microcystis aeruginosa* grows in quantities and *sundaicus* dis appears It is thus seen that the salt water form breeds largely in polluted waters and the fresh water form in clean waters, which may be a significant difference in their behaviour

Covell and Singh (1942) observed the association of *sundaicus* with thirteen types of aquatic plants and eight types of algæ, Najas, Ceratophyllum and Hydrilla among plants and Lyngbya, Anabena and Spirogyra among algæ being the most important In fresh waters, association with the same three plants and Spirogyra was very marked Whereas a thick cover of *Eichhornia speciosa* in the breeding place was found to inhibit *sundaicus* breeding in Bengal (Iyengar, 1946),

places both by Covell and Singh (1942) and Venkat Rao and Ramakrishna (1947*a*)

Control of *sundaicus* breeding may be effected by the use of paris green or naturalistic measures like deweeding Paris green treatment of the numerous breeding places at intervals of five to six days is a very costly and difficult method It is also likely to be inefficient during periods of heavy and continuous rainfall Deweeding thus becomes the only reliable alternative available

Deweeding by manual and other mechanical means was tried on a large scale in the Chilka and North Vizagapatam areas and proved very effective The breeding is immediately checked and the breeding places remain negative for *sundaicus* larvæ as long as the weed free condition of the water surface is maintained However, regrowth of vegetation occurs so fast, at least during the first two or three years, that the maintenance work becomes very difficult, requiring a large labour force and proper supervision, without which the work becomes unsatisfactory

A very much simpler and equally effective method of deweeding is offered by the recent introduction of chemical weed killers These are claimed to remain effective, after one application, for four to five years, in which case one application may suffice for the whole campaign

While this method is applicable to inland waters, both fresh and saline, of limited extent, it does not apply, owing to its cost, to the large bodies of salt water like the Chilka Lake, which alone is over 500 square miles in extent But, in this

lake, though the fauna is marine, the flora is that of fresh water (Annandale and Kemp, 1915), which can be eliminated by raising the salinity through the introduction of sea water. There ma
vicinity of the lake where th
irrigating the ricefields but
fish supply, for which the l
necessary to keep the mouth of the lake constantly open for the ingress of sea water, as otherwise the littoral sand drift might soon choke the mouth, resulting in the ultimate freshening of water in the lake.

Lastly, effective measures have to be undertaken to prevent re-infestation from the neighbouring countries, East Pakistan and Burma. It is now recognized that, for eradication of malaria or of vector anophelines, international cooperation is essential. The best method would appear to be the application of eradication measures simultaneously in all the three countries

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SOME MALARIA ERADICATION PROBLEMS AS VISUALIZED IN 1955

BY

F J PAMPANA, M D

(Chief, Malaria Section, World Health Organization)

(August 25, 1955)

"The ultimate goal of a nation wide malaria control programme is the eradication of the disease" —*W H O Second Asian Malaria Conference*, 1954

It seems strange that during the many years of malaria control by residual insecticides so little account has been taken of the destiny of the malaria parasite in man Attention has been focused on vector control, apparently forgetting that if the vectors have no infection to transmit, their control would be superfluous The fact that malaria infections die out spontaneously within a few years and that therefore, if no new cases occur or are imported, the population will be cleared of malaria when those few years are over, was very seldom taken into consideration when planning programmes During the development of a programme, emphasis was put on operational techniques, on the number of houses sprayed, on variations of vector densities, less frequently on those of malariometric rates, but practically never on achieving the full interruption of transmission which might have led to the eradication of the infection in the population and to the discontinuation of insecticide spraying This concept was presented as far back as 1948 at the Fourth International Congress of Tropical Medicine and Malaria (Pampana, 1948, 1952), but it was only after the demonstration that some anopheline species could develop resistance to chlorinated hydrocarbon insecticides that it was given serious consideration It was then felt that resistance was such a danger that efforts should be made to shift the objective of antimalaria activities from simple malaria control, that is reduction of transmission, to malaria eradication, so that residual insecticide applications could be stopped before resistance had a chance to occur (Pampana, 1954) This principle was discussed and a new strategy eventually approved by important international conferences, both at the inter-governmental level (XIV Pan-American Sanitary Conference Santiago, 1954) and at the technical level (Second Asian Malaria Conference, Baguio P I, 1954) and, finally, by the Executive Board (15th Session) of the World Health Organization

in January 1955 and the Eighth World Health Assembly (Mexico, May 1955) While readers of this Journal are probably acquainted with the Report of the Second Asian Malaria Conference, it might be useful to recollect that the Santiago Conference resolved "that it [was] of the utmost urgency that the Member

of nation-wide malaria control so that malaria eradication may be achieved and the regular insecticide-spraying campaigns safely terminated before the potential danger of a development of resistance to insecticides in anopheline vector species materializes" It may be said that there is today a large consensus of expert opinion that wherever it is planned to control malaria by residual insecticide spraying, eradication of the disease should be the goal, so that the insecticide could be discontinued when *still fully effective against the vectors* Obviously *eradication*

finance

iments

would

require a larger *annual budget than present* control programmes, this *would* only be required for a few years, so that in the end savings would be effected, and (2) that by continuing residual spraying from year to year resistance to the insecticides might develop and malaria control would then become a much more expensive proposition, if not practically impossible

But even malariologists, not to mention public health administrators, may have some doubts as to the advisability, the feasibility and the urgency of malaria eradication These doubts are quite understandable, for eradication *is a new* venture We shall try in this paper to foresee some of these queries and doubts, and attempt to reply

1 One of the reasons that prompt us to change our strategy is the development of resistance to insecticides Is it likely that resistance, so far described only in a few species in a few countries or localities, would develop in others? Unfortunately there is perhaps no answer to this first query But this same question came to the mind of malariologists after the report of the D D T resistance of *A sacharovi* in Greece (Livadas, 1951, Livadas and Georgopoulos, 1953) Later also in the same country *A maculipennis* and *A superpictus* were reported to have developed resistance as well (Belios, 1954) A few months passed Then in some localities of Java *A sundaicus* it was demonstrated (Crandell, 1954), had become D D T resistant More months passed, and then resistance was stated to have developed in *A stephensi* in some localities of Saudi Arabia (Daggy, 1955) If this has happened, it seems reasonable to think that in the future resistance may occur in other parts of the world and with other species And as resistance to the chlorinated hydrocarbon insecticides might be, in our present state of knowledge, a very serious occurrence in countries which were highly malarious before the inception of control, there is ample justification for adjusting programmes in such a way as to obtain most benefit from the insecticides and to stop their application when they are still active

2 It is stated that malaria eradication is possible because malaria infections are self curing and do not last more than three years But we all know of ancient

[illegible]

falciparum [illegible]
nine to twelve months has been
in experimental infections with a
however 279 5 days (±19 9) (Je [illegible] months in
Porto R[illegible]

[illegible]

As regards *vivax* infections which generally do not last beyond two years we shall only recollect observations on infections contracted in the South Pacific in 4 3 per cent of which clinical attacks were still present four years after (Hill and Amatuzio 1949)

In conclusion there certainly are infections of *P falciparum* lasting more than one year and of *P vivax* lasting more than three years This is a parasitological truth such cases however are rare* and we may assume, for public health purposes that they do not invalidate the general statement that if no new cases of malaria have occurred for three years in a given locality, its population no longer represents a source of infection for anophelines It should not be forgotten that public health policies are based on generalizations No vaccination gives 100 per cent protection and still vaccination has succeeded in eradicating smallpox from many a country

If exceptionally a long lasting malaria infection succeeds in infecting a mosquito and in giving rise to secondary cases the small outbreak could easily be brought under control particularly so if residual insecticides can be effectively employed It might be compared to an outcrop of secondary cases following the immigration from abroad of a gametocyte carrier such as that described by Brunetti *et al* (1954) in the U S A

3 When could it be stated that malaria eradication has been achieved? We know that among the various malariometric indices the infant parasite rate (I P R) [illegible]
ter
fav
aft
cor
fou [illegible] Case (*a*) of Figure 1 depicts this example Of course, a zero infant parasite rate does not necessarily mean that no cases occur in the population,

* In this connexion it may be interes[illegible]

therefore, we cannot say that malaria eradication has been achieved when we stop the insecticide It will be necessary first to set up a machinery of searching for he necessary protective measures This should be set up, as recommended by re the discontinuation of spraying We should assume that, as in our figure, it is working already in the year which is supposed to be the last of the spraying years In other words, in the first example (*a*) of Figure 1, in the third year of spraying, in the second example (*b*), in the fourt year Now let us recollect the definition of the National Malaria Society of the U S A " Malaria may be assumed to be no longer endemic in any given area when here for three years, if reporting adequate investigations are carried nition which had been quoted by the Fifth Report of the Expert Committee on Malaria of WHO) is that *when malaria " is no longer endemic "* in any given area, it would mean that eradication had been achieved three years before In case (*a*) of Figure 1 eradica *tion would have been obtained in the fourth year, in case (b) in the sixth year* In conclusion the date of actual eradication could only be established retroactively

4 It has often been recommended that the area of eradication should be " as large as possible ' (Reports of the First and of the Second Asian Malaria Conferences) One would think it easier to eradicate malaria from a village or a group of villages rather than from a whole country But it would be impossible to maintain those localities free of sources of infection for the vector mosquitoes because we can neither compel the villagers to remain for at least three years in their villages, nor preclude the entrance of other people from outside It might be possible to prevent such exchange of persons if the villages were completely isolated, as, for instance, in the case of an island With such exceptions, the large *size of an area would minimize the danger of sources of infection being imported* The larger the area is, the smaller would be the danger Eradication on a continental scale, as it has been decided for the Americas, once achieved, will have to establish protection only against travellers coming from other continents or oceanic islands

Still, in programmes on a continental, sub continental or even country wide scale, it might be expedient and even necessary to proceed by steps and to split the territory from which malaria should be eradicated into zones with different priorities Each of these zones should, as far as possible, be large enough to reach the borders of healthy areas, or natural, or man made barriers so that the reintroduction of sources of infection would be minimized In some cases this might not be feasible, and one might suggest continuing the residual spraying of all localities situated at the periphery of the eradication area But the danger of developing insecticide resistance would counterindicate this idea, which, in any case, would hardly be logical

5 Still, if the eradication area cannot be surrounded by healthy areas or adequate barriers, some way could be devised to reduce the danger of reintroduction of sources of infection

Let us suppose that, contiguous to eradication area '*A*' is another malarious area '*B*' and that the epidemiological conditions in '*A*' are such that it can be

FIGURE 1

Tentative schemes of the sequence of events in malaria eradication programmes

Years	-1	1°	2°	3°	4°	5°	6°	7°	8°	9°	10°
Case (*a*) of conditions exceptionally favourable in which the infant parasite rate in infants born after the first spraying is brought down to naught during the first year											
	SURVEY	ATTACK	CONSOLIDATION		MAINTENANCE						
Spraying operations (on a total coverage base)		xxxxxxxxxxxxxxxxxx									
Infant parasite rate	++	o(1)	o	o							
Epidemiological surveillance				XXXXXXXXXXXXXXXX Special surveillance carried out by malaria service				General surveillance carried out by health service			
New cases of malaria locally contracted and traced by epidemiological surveillance				++	o	o	o	↑ At this point malaria is no longer endemic			
Case (*b*) of average conditions rather favourable in which the infant parasite rate is brought down to naught only during the second year of spraying											
	SURVEY	ATTACK	CONSOLIDATION			MAINTENANCE					
Spraying operations (on a total coverage base)		xxxxxxxxxxxxxxxxxxxxxxxxxx									
Infant parasite rate	++	+(1)	o	o	o						
Epidemiological surveillance					XXXXXXXXXXXXXXXXXX Special surveillance carried out by malaria service					General surveillance carried out by health service	
New cases of malaria locally contracted and traced by epidemiological surveillance	(?)	(?)	(?)	(?)	+	+	o	o	o	↑ At this point malaria is no longer endemic	

(1) In infants born after first spraying

foreseen that spraying can be withheld after four years of operations It will be recollected that the Second Asian Malaria Conference agreed that "adequate surveillance of malaria incidence should be initiated well before the time of interruption of spraying". Then in area '*A*' surveillance should be functioning not later than during the fourth year Suppose that we provide, in the country-wide programme, for expansion of the operations to area '*B*' in this same year Then a very large proportion of, if not all, new malaria cases in '*B*' will be prevented in the year What will then be the reservoir of infections during the fourth year in '*B*'? Very few *falciparum* subjects, infected prior to the spraying, will still show parasites There will, however, be a good proportion of sources of infections of *P vivax* and of course of *P malariæ*, contracted chiefly prior to the beginning of

s

in the fifth year) not many could be capable of infecting the anopheles of '*A*' Moreover, as epidemiological surveillance in '*A*' is already functioning, malaria cases both in immigrants from '*B*' and in inhabitants of '*A*' (who might have become secondarily infected from the former) could be easily traced and dealt with Finally, if spraying of '*B*' in the fourth year reduces, on the one hand, the problem which faces epidemiological surveillance of '*A*' it will also, on the other hand, protect visitors from '*A*' from getting infected in '*B*' and carry back the infection to zone '*A*'

In conclusion, even if no adequate, natural or man-made barrier could be found, it would appear that a satisfactory protection might be secured, if, in a

tart simultaneously (if not earlier)

foreseen and if in the same year

ed

6 As the possibility of starting transmission again after spraying is discontinued appears as a real danger, it would be interesting to visualize how dangerous the immigration of people from malarious areas of varying endemicity into the area from which spraying has been stopped, would be If we call '*A*' the area in which spraying has been stopped, let us call '*B*' and '*C*' the surrounding areas, which are both malarious '*B*' is hyperendemic, or holoendemic Everyone of its people will probably be infected, but gametocytes will be found practically only in the blood of children Now children, introduced in area '*A*' would represent a great danger for infecting the local mosquitoes, but children travel much less than adults, and only a few would be likely to be brought into area '*A*', moreover, they could be easily spotted, by the surveillance teams, and efficiently treated

Area '*C*' on the other hand, is a mild meso-endemic area, let us suppose with a spleen rate of 20 per cent Here we would probably find gametocytes carriers among adults, but infected subjects, whatever their age, would represent only a small proportion of the total population In the cases of both '*B*' and '*C*', therefore, the danger represented by immigration of people from malarious areas into the adjoining eradication area (if this is sufficiently large and adequately

supervised by epidemiological surveillance) is perhaps less than one would think The danger would be greater for persons of '*A*' visiting '*C*' and particularly '*B*', but one would think that these persons should they develop malaria upon their return, would more easily be found by the personnel of the epidemiological surveillance and one would count on their willingness to co-operate with them

The mode of travel across the borders of the eradication area also deserves attention Travelling on foot, by horse, or ox-cart, by bicycle, etc, represents probably the greatest menace because these are the means employed by rural groups, such as entire families going from village to village This method of travel however, does not generally cover long distances* and if the eradication area is large enough it would represent a danger only for the peripheral band where epidemiological surveillance should therefore be particularly efficient Travelling by other means motor bus or train is expensive over long distances babies and children do not travel alone, and the travel of entire families by these means would perhaps not be too frequent and might be restricted to cases of change of residence, important family events etc Furthermore one would think that most of the people travelling long distances by train would come from towns and go to live in other towns, and towns often have no anophelines or else are the first localities in which malaria is controlled This reasoning applies even more cogently to those travelling by air

In conclusion it appears that if the eradication programme covers an area large enough and if epidemiological surveillance is more efficient and strict in the peripheral part of it, the problem of imported gametocyte-carriers could be solved satisfactorily

7 As shown in Figure 1 it is tentatively assumed that residual spraying may be interrupted obviously with the necessary safeguards after the infant parasite rate has remained at zero for three years In order to shorten as much as possible the period of years during which insecticide spraying must be carried out, efforts should be made to bring the I P R down to zero rapidly In WHO's experience this may happen after the first spraying but only exceptionally More often two years of spraying at least will be necessary In other cases this is not enough, or in some areas the I P R becomes zero only in some sectors and not in others Often such failures can be explained by the small size of the area or by disregard of the need of total coverage or by faulty techniques (including poor insecticide formulations or rapid sorption of the insecticides by the walls) Should these three mistakes be corrected or avoided and transmission continue then it may be thought that transmission is occurring at least in part outdoors By repeating the spraying from year to year it is to be expected that the progressive reduction of gametocyte-carriers in the population would eventually stop transmission, but given the advisability of accelerating results with a view to discontinuing spraying before resistance may occur it will be necessary to supplement residual spraying with other anti malaria techniques such as

(*a*) Anti imago space spraying such as was applied before the D D T era in South Africa in India, in the Netherlands

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*It will be noted that in this paper we have refrained from discussing the difficulties caused by nomadism which is a special case and could not be sufficiently dealt with in this short article

(*b*) Larval control, though excluding the use of the chlorinated hydrocarbon insecticides

(*c*) Use of drugs Very exceptionally would it be possible to submit a whole population of an area to frequently repeated administrations of drugs, for the organization of such schemes would be very difficult and costly, but ways could be found of utilizing the spraying personnel for distributing a few mass treatments to all or to selected groups of the population

The use of drugs might also be considered in areas where the residual insecticide will succeed in fully interrupting transmission, with a view to reducing the number of years during which the insecticide spraying must be continued It is realized, however, that with the possible exception of Pinotti's (1953) method, the systematic distribution of drugs or a systematic attempt towards radical cure of all cases of *vivax* or *malariæ* infections will be a very difficult problem

8 In programmes aiming simply at some degree of malaria control, it is not essential, although desirable, to cover by residual spraying (or possibly to protect by other means) all houses of the area In *programmes aiming at malaria* eradication total coverage is essential Furthermore, if interruption of the spraying is to be applied as soon as possible, not only total coverage will be essential, but also a simultaneous implementation of the programme all over the area, with the same degree of efficiency everywhere (This need of coordination in space, time and efficiency was emphasized in the Report of the Second Asian Malaria Conference) These are, incidentally, the reasons why eradication programmes have a higher *per capita* cost than control programmes If in some portions of the area people refuse to have their houses sprayed, or if in some [illegible] take *them*, [illegible] cessary [illegible] e been foreseen had the reaction of the population been more favourable Hence the need of providing for a suitable education of the population on the one hand, and, on the other hand, for suitable legislation

Legislation for malaria eradication should not only provide authority to overcome the objections of the inhabitants where health education has failed, but, as for instance in countries where the operations are largely decentralized, should also make provision for allowing the central antimalaria organization to intervene if the local authorities are lagging behind the schedule of the national endeavour in which they participate

SUMMARY

As it appears that there is to day a large consensus of expert opinion that the objective of malaria control by residual insecticide spraying should be that of malaria eradication, so that the spraying of insecticide could be discontinued before the local vectors develop resistance to it, some problems related to eradication have been considered These problems are, whether D D T resistance is likely to develop in future in other species, whether it is correct that from the public health standpoint eradication of the infection can be achieved after a few years,

and when. The questions of the size of the area and of the danger of reintroduction of the sources of infection in the area from which malaria has been eradicated, and the influence of the mode of travel on this danger have been considered.

Finally, techniques supplementary to insecticide residual spraying are suggested to control pockets where transmission may linger, and the need of adequate legislation in any eradication campaign is emphasized.

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OBSERVATIONS ON SOME ASPECTS OF THE NOCTURNAL BEHAVIOUR OF *ANOPHELES CULICIFACIES*

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INTRODUCTION

This paper reports observations made on some aspects of the nocturnal behaviour of *Anopheles culicifacies*, the most important vector species involved in malaria transmission in India. Such studies throw light not only on the normal pattern of behaviour of the adult mosquitoes but on possible changes which may follow the application of residual insecticides. The insect behaviour vitally affects the degree and duration of successful establishment of malaria control and, ultimately, malaria eradication. Insect behaviour not only varies with species as shown by Thomson (1950) in East Africa, Davidson (1953) in Kenya, Wharton (1951) in Malaya and Bordas and Downs (1951) in Mexico, but also with respect to the same species in different geographical areas as shown in the case of *A. fluviatilis* in India, by Nursing, Rao and Sweet (1934) in Mysore, Viswanathan, Ramachandra Rao and Rama Rao (1944) in N. Kanara District (Bombay State), Senior White, Ghosh and Venkat Rao (1945) in Orissa and Jaswant Singh and Mohan (1951) in the Nilgiris (Madras State). *A. culicifacies* is much more widely prevalent in India and transmits malaria in widely separated regions and its pattern of behaviour is, therefore, likely to be more varied. While several studies on certain aspects of the bionomics of adult *A. culicifacies*, such as those relating to resting places, feeding habits, hosts of predilection, longevity, range of flight, ovipositing behaviour, etc., have been published, there are few records on the nocturnal behaviour. Even the few that have been published are based on limited observations (Rajindar Pal, 1945, Rajindar Pal and Sharma, 1952).

METHODS

Two experimental huts were constructed for the purpose of these studies at Vithalwadi located on the banks of the Mutha River, six miles to the west of Poona City The river bed itself and several small streams, channels and seepages in the locality provided good breeding places for *A culicifacies* The huts (Figures 1 and 2) were 8 feet long and 6 feet broad and had gabled roofs, the highest point of which was 7½ feet from the ground The walls and roof were made of bamboo matting supported by strong bamboos at the corners The roof was covered by thatch and the inner sides of both the roof and the walls were completely lined with mud plaster The hut had one door 5 feet × 2 feet facing east and only one window 1 foot square on the north The door could be closed fairly tightly The window was provided on its exterior with an outlet window trap made of cloth netting On two sides of the hut, across the middle, was a horizontal opening produced by the overlapping of the upper part of the matting over the lower part, the space between the two being about two inches The extent of the overlap was four inches, and a mosquito in order to enter the hut through these openings had to fly four inches upwards before reaching the interior When the door was tightly shut, the only entrance available for the mosquitoes was through these long slits In view of the well known tendency of mosquitoes not to fly downwards when trying to escape, these slits provided possible means of ingress when the door was kept shut but not for their egress The dimensions of the hut were such that the entire interior could be thoroughly inspected and all resting mosquitoes easily



Fig 1 Experimental huts built for the study of behaviour of *A culicifacies*

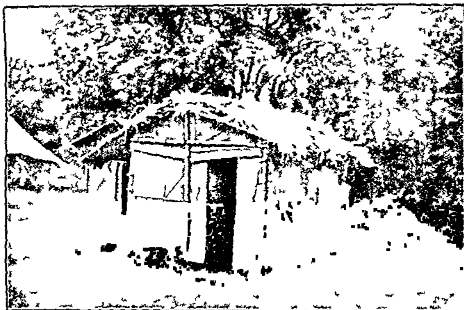


Fig 2 Closer view of one hut showing the window trap The arrow points to the slit entrance

collected by hand with the suction tube A tent was pitched 50 feet away from the huts to provide a small field laboratory for use at night Except for a couple of rural houses about 300 yards away there were no other houses within a radius of half a mile

A buffalo was tethered in the hut between 18 00 and 07 00 hours on every night of observation Several preliminary attempts with human baits showed [illegible]

necessary to be able to spot dead insects

OBSERVATIONS

Observations were made in these huts on the time of entry and the time of feeding from December 1951 to May 1952 and on the effects of D D T spraying *in June November and December 1952 During the monsoon months no* observations were made

MOSQUITO FAUNA

During the course of these studies adults of the following species of mosquitoes were collected in the huts —

Anopheles
1 *annularis*,
2 *culicifacies*,
3 *fluviatilis*,
4 *hyrcanus*,
5 *jamesi*,
6 *jeyporiensis*,
7 *stephensi*,
8 *splendidus*,
9 *subpictus*,
10 *tessellatus*,
11 *theobaldi*
12 *turkhudi*, and
13 *vagus*

Culex
1 *bitaeniorhynchus*,
2 *fatigans*, and
3 *vishnui*

Further studies were, however, restricted only to *A culicifacies*

TIME OF ENTRY

In order to determine the time of entry, a thorough search was first made in the huts between 17 30 and 18 00 hours and all resting mosquitoes removed by hand collection Captures were then made in the huts every three hours by two trained Insect Collectors working simultaneously for thirty minutes, that is, between 20 30 and 21 00 hours, 23 30 and midnight, 02 30 and 03 00 hours and 05 30 and 06 00 hours Again, a further search was invariably made between 07 00 and 07 30 hours to collect any mosquitoes which had entered the hut subsequent to the search made between 05 30 and 06 00 hours This time schedule was observed in all seasons of the year

In a series of 54 observations made with the door fully closed, the total number of *A culicifacies* collected in these huts was 492 out of which 447 were females (Table I) and in another series of 27 comparative observations made with the door fully open 311 males and 1,118 females of this species, or 1,429 in all, were collected The figures bring out the fact that nearly five times as many female *A culicifacies* enter the huts when the door is kept open as when only the slit entrances are available

Observations made in the three-hourly collections were compared with another series of observations in which catches were made only once between 07 00 and 07 30 hours The data collected in 18 observations with the door closed and 17 with the door open, are given in Table II Many of these observations were made on nights alternating with those in which three hourly catches were made and therefore, the data are generally comparable and the seasonal differences in the output from the breeding places do not differently affect the two types of observations These figures reveal that when the door is kept open, the average number of *A culicifacies* when only a single collection is made in the morning is

26 5 females and 11·6 males as compared with 41 3 and 11 6, respectively, when catches are made once in three hours and again in the early morning indicating that most probably a certain proportion—roughly 36 per cent—of *A culicifacies* females which enter the hut during the night and dawn leave the hut before, say, 1 30 hours But when the door is kept closed, there is no outward movement during the night as shown by the average number collected in the single early morning catch (11 3) not being less than the total of all the quarterly collections plus the early morning catch (8 3) These figures are in accordance with the view that the slit entrances while affording ingress to the mosquitoes are not suitable for their egress

TABLE I

Number of A culicifacies *collected in four 3 hourly collections and at 07 00 hours*

	With door closed.	With door open
Number of nights of observation December 1951 to May 1952	54	[illegible]
Total number of *A culicifacies* collected in all the four 3 hourly collections and at 07 00 hours		
Males	45	211
Females	447	1 118
Average number collected per nigh		
Males	0 8	11 6
Females	8 3	41 3

TABLE II

Number of A culicifacies *collected in single catches made at 07 00 07 30 hours*

	Door closed	Door open
Number of observation	18	1
Total number of *A culicifacies* collected in single catches made at 07 00-07 30 hours December 1951 to May 1952		
Males	11	19
Females	5 4	431
Average number collected per night		
Males	[illegible]	11 6
Females	11 3	[illegible] 5

In Table III are given figures regarding the number and proportions of females of *A culicifacies* entering the hut at the different quarters of the night

and the early [illegible]
observations
study Of th[illegible]
second quarter, making a total of 90 per cent entering before midnight Similarly of the 1,118 females collected in 27 nights when the door was kept open, 44 per cent entered in the first quarter and 23 per cent in the second quarter, making total of 67 per cent of entry before midnight These figures bring out the fact that while *A culicifacies* enter dwellings throughout the night, the bulk of entry occurs before midnight and that the first quarter is the most active period of entry The figures further suggest that a certain proportion of those which enter houses in the earlier part of the night, leave them and re enter later Thus in the first quarter nearly 30 out of 74 or roughly 40 per cent leave the houses presumably in search of more congenial places of feeding or shelter In the first and second quarters put together 23 out of 90 or roughly 25 per cent leave the houses This shows that at least 7 out of the 30 mosquitoes which left the houses out of a batch of 74 which entered during the first quarter, re-entered during the second quarter Only about ten per cent enter houses for the first time after midnight

TABLE III

Number and proportions of females of A culicifacies *entering the hut at different quarters of the night and the early morning*

	Door closed		Door open	
Number of nights of observations	[illegible]4		27	
Females of *A culicifacies* captured in	Number	Per cent	Number	Per cent
1st quarter	[illegible]	74	[illegible]	44
2nd quarter	1	16	[illegible]	23
3rd quarter	9	[illegible]	83	[illegible]
4th quarter	19	4	[illegible]	14
07 00-07 30 hours	19	4	140	1[illegible]
Total	44	100	1 118	100

TIME OF FEEDING

In Table IV are presented figures showing the proportions of female A [illegible] e of capture These [illegible] lled observations on [illegible] The classification of [illegible] sed by Viswanathan [illegible] ion of the classes *A* and *B*

TABLE IV.

Proportions of A. culicifacies females in different gonotrophic conditions

(A) IN COLLECTIONS MADE AT 3 HOURLY INTERVALS AND AT 07.00-07.30 HOURS

Number of nights of observations	Door closed							Door open						
	14							18*						
	Percentages							Percentages						
	Total	A	B	C	D	E	F	Total	A	B	C	D	E	F
1st quarter	319	0	78	12	2	0	2	443	11	58	29	@	0	@
2nd quarter	71	1	83	11	1	0	3	154	7	81	12	0	0	0
3rd quarter	9	0	67	33	0	0	0	30	0	93	7	0	0	0
4th quarter	19	0	68	[illegible]	16	0	10	68	23	[illegible]	8	1	0	[illegible]
07.00-07.30 hours	19	6	58	16	10	5	0	[illegible]	26	41	24	6	0	0
Total	447	3	78	12	3	@	2	746	14	64	22	@	0	@

@ = Less than 1 per cent

(B) IN COLLECTION MADE ONLY AT 07.00-07.30 HOURS

Number of nights of observations	18							[illegible]						
	Percentages							Percentages						
	Total	A	B	C	D	E	F	Total	A	B	C	D	E	F
Total	[illegible]	2	75	10	3	2	5	147	1	57	41	1	[illegible]	0

* *Note*.—The data for nine collections made in May 1952 not included as they are incomplete *in respect of gonotrophic conditions*.

The classification now used is as follows :—

Class *A* Empty abdomen, unfed

- *A1* With no trace of old blood
- *A2* With traces of previous bloodmeal

Class *B* Freshly fed

- *B1* Fully fed no trace of old blood, or of ovarian development
- *B2* Fully fed with trace of old blood but no ovarian development
- *B3* Fully or partially fed with traces of old partially digested blood and of ovarian development
- *B4* Partially fed without trace of old blood or of ovarian development (interrupted feeding)

[illegible] In the 54 completed [illegible]

second quarter, making a total of 90 per cent entering before midnight Similarly, of the 1,118 females collected in 27 nights when the door was kept open, 44 per [illegible] ond quarter, making a [illegible] bring out the fact that [illegible] ie bulk of entry occurs [illegible] period of entry The [illegible] ich enter houses in the [illegible] hus in the first quarter nearly 30 out of 74 or roughly 40 per cent leave the houses presumably in search of more congenial places of feeding or shelter In the first and second quarters put together 23 out of 90 or roughly 25 per cent leave the houses This shows that at least 7 out of the 30 mosquitoes which left the houses out of a batch of 74 which entered during the first quarter, re-entered during the second quarter Only about ten per cent enter houses for the first time after midnight

TABLE III

Number and proportions of females of A culicifacies *entering the hut at different quarters of the night and the early morning*

	Door closed		Door open	
Number of nights of observations	54		27	
Females of *A culicifacies* captured in	Number	Per cent	Number	Per cent
1st quarter	329	74	490	44
2nd quarter	71	16	254	23
3rd quarter	9	2	83	7
4th quarter	19	4	151	14
07 00-07 30 hours	19	4	140	12
Total	447	100	1 118	100

TIME OF FEEDING

In Table IV are presented figures showing the proportions of female *A culicifacies* found in different gonotrophic conditions at the time of capture These [illegible] Table III as detailed observations on [illegible] in every case The classification of [illegible] udies is the one used by Viswanathan and Ramachandra Rao (1944) [illegible] her sub-classification of the classes *A* and *B*

TABLE IV.

Proportions of A. culicifacies *females in different gonotrophic conditions*

(A) IN COLLECTIONS MADE AT 3 HOURLY INTERVALS AND AT 07 00-07 30 HOURS

Number of nights of observations	Door closed							Door open						
	34							18*						
	Percentages							Percentages						
	Total	*A*	*B*	*C*	*D*	*E*	*F*	Total	*A*	*B*	*C*	*D*	*E*	*F*
1st quarter	319	6	78	12	2	0	2	443	14	56	29	@	0	@
2nd quarter	71	1	83	11	1	0	3	154	7	81	12	0	0	0
3rd quarter	9	0	67	33	0	0	0	30	0	93	7	0	0	0
4th quarter	19	0	68	5	16	0	10	66	23	68	8	1	0	0
07 00-07 30 hours	19	6	58	16	10	5	0	53	26	44	24	6	0	0
Total	447	5	78	12	3	@	2	746	14	64	22	@	0	@

@ = Less than 1 per cent

(*B*) IN COLLECTION MADE ONLY AT 07 00-07 30 HOURS

Number of nights of observations	18							7						
	Percentages							Percentages						
	Total	*A*	*B*	*C*	*D.*	*E*	*F*	Total	*A*	*B*	*C*	*D*	*E*	*F*
Total	204	2	75	10	5	2	5	117	1	57	41	1	0	0

**Note*—The data for nine collections made in May 1952 not included as they are incomplete in respect of gonotrophic conditions

The classification now used is as follows —

Class *A*. Empty abdomen, unfed
- *A1* With no trace of old blood.
- *A2* With traces of previous bloodmeal

Class *B*. Freshly fed
- *B1* Fully fed, no trace of old blood, or of ovarian development
- *B2* Fully fed, with trace of old blood but no ovarian development
- *B3* Fully or partially fed with traces of old partially digested blood and of ovarian development
- *B4* Partially fed without trace of old blood or of ovarian development (interrupted feeding)

Class *C*	Partially digested blood and partial ovarian development		
Class *D*	Gravid, with a slight trace of old blood		
Class *E*	Gravid, without trace of blood		
Class *F*	Miscellaneous	*F1*	Unclassified
		F2	Partial digestion of blood but no ovarian development

For purpose of Table IV, however, the sub classifications of *A* and *B* are not used

It will be noticed that 78 per cent of all females caught with the door closed and 64 per cent with the door open belong to the Class *B* that is those which had taken fresh bloodmeals With the door closed, the proportions of specimens

proportion of freshly fed specimens in the first and last quarters than in the second and third This may be due to the exercise of a greater degree of choice by the mosquitoes resulting in some movement of mosquitoes ready to feed to other possible places of feeding Altogether while feeding may take place all through the night, generally it occurs soon after entry and as the bulk of the entry takes place before midnight the bulk of feeding also occurs before midnight

The data also show that a certain number of females in the *C* and *D* classes also enter the huts their total proportions being as much as 15 per cent in the closed door hut and 23 per cent in the open door hut When a single collection was made at 07 00 07 30 hours their proportions were 15 per cent with the door clo

in

not

classes collected been largely restricted to the 07 00 07 30 hours collection, one might have explained it as due to the entry of shelter seekers at daybreak But the entry of the *C* and *D* classes throughout the night indicates either that there is a

second feeding before their first ovip

the proportion of the *C* and *D* clas

hut while it is only 15 per cent in

feeding is greater and stimulates entry even with obstacles while the urge for shelter seeking is not so great as to surmount difficulties in entry

In Table V are given the sub classifications of 1,942 freshly fed *A culicifacies* (Class *B*) females collected in all the captures made in these huts and in which such data were recorded including also the 447 and 746 females which were dealt with above Of the 1,942 females subjected to this analysis, 61 per cent were in

B1 condition 19 6 in *B2* 7 1 in B3 and 12 3 in *B4* From the details of the classification presented earlier it will be seen that only *B1* *B2* and *B4* are forms which actually enter the huts in *A* condition that is in an unfed condition with

ondition and They form lmeal on the r cent of the iales for the iposed partly on behaviour

are roughly 12 per cent of the again during the same night to complete their bloodmeals No significant variations in these proportions have been noticed between the different months The feeding by a proportion of the semi gravid mosquitoes within a gonotrophic cycle somewhat increases Macdonald s (1950) biting index unless in the case of parous females those that bite more than once have their gonotrophic cycle extended at least during that cycle In the case of nulliparous females the duration between emergence and oviposition is shown by Davidson and Draper (1953) to be at least twice as long as subsequent gonotrophic cycles Hence the biting frequency is not altered Multiple feeding in the same night by a mosquito on different hosts profoundly affects transmission the definite extent of which has not yet been precisely determined

TABLE V

Classification of freshly fed females of A culicifacies *in respect of all collections from January to end of May*

Month	B	B	B_3	B_4	Total
Jan ary	53	18		11	110
February	183	43	5		303
March	37	4	3	4	394
Apr l	4	11	9	8	81
Ma	341	1	33	58	534
To al	1 4	381	138	239	1 949
Per cent		6	1	1? 3	10

OUTLET WINDOW TRAP

The number of mosquitoes c ll cted in the outlet window traps throughout the period of these stud es was very small and extremely disappointing During the entire period of study with over 00 nights of observations in unsprayed huts only 33 adults of *A culicifa ie* 16 males and 17 females) were found The outlet window traps were therefor not considered of much utility in the study of behaviour of this species

DEGREE OF OUT-DOOR RESTING

The observations made in the huts have also not yielded any definite information regarding the degree of outdoor resting during daytime resorted to by adults of *A culicifacies* While from a comparison of the number of mosquitoes collected in the three hourly collections and the single collection made in the morning it has been inferred that roughly 36 per cent of *A culicifacies* leave the dwellings at night, this movement may only be directed towards finding a better place of feeding or shelter A fair number enter the dwellings in the early morning Unless the relative numbers which actually leave the huts at night and those which enter the hut in the morning are adequately determined it would not be possible to estimate the proportion whi
of the relative proportions of
early morning collections (T
semi gravid females resting indoors is only slightly less than the number of freshly fed ones and the difference may be due to the natural mortality taking place It should be remembered that all the mosquitoes reported in these studies were those which entered the hut during single nights, for the huts were thoroughly searched

days cannot be stated From the first glance of these figures one may conclude that as the gonotrophic cycle is 48 hours practically all the females are endophilic but this will be true only if collections made in dwellings represent the total insect population Further studies are needed in this regard

BEHAVIOUR IN HUTS SPRAYED WITH D D T

Several preliminary attempts were made to study the behaviour of mosquitoes in huts treated with D D T One hut was sprayed on May 23, 1952 at a dosage of 112 mg /sq ft in an aromex water emulsion and observations carried on for 11 nights thereafter till the onset of the monsoon After the monsoon the huts were rebuilt and one of them was sprayed on November 14, 1952 at a dosage of 56 mg /sq ft again is an aromex water emulsion and observations were carried on for six days thereafter The observations in these two huts are described below

(1) *Hut sprayed on May* 23, 1952 —No separate studies were made in this hut just prior to the spraying but the normal behaviour of the mosquitoes in unsprayed huts as described above, held good Collections, made on 11 consecutive nights after the day of spraying, consisted of (*i*) mosquitoes resting inside the hut (*ii*) mosquitoes found dead on the floor and (*iii*) mosquitoes found in the outlet window trap In all these observations the door was kept closed and only a single collection made at 07 00 07 30 hours It was soon realized that the number of mosquitoes found dead on the floor did not represent all the dead ones because of the interference by the buffalo which was used as a bait Therefore, the data in respect of this hut cannot be used for quantitative studies but can be employed for qualitative purposes only In all these collections only two live *A culicifacies*,

females both in the unfed condition were found resting in the hut Perhaps they h[illegible] entered the hut just prior to the collection Eight males and 12 females of t[illegible] Of the 12 females 9 were unfed and [illegible]

A culi[illegible] e
numb[illegible] e
traps [illegible] enomenon of excito repellancy but all those found [illegible] therefore the number which escape death is perhaps insignificant

(2) *Hut sprayed on November 14 1952* —Preliminary observations were made on four nights before this hut was sprayed in two of which quarterly collections were made and in the other two only a single collection in the morning was made In all these observations the door was kept open The results of these collections were as follows

(*A*) *Single collection at 07 00 07 30 hours —Two observations —*

	Males	Females
A culicifacies	0	8(*B*-6, *C* 2)

(*B*) *Quarterly collections—Two observations —*

	Males	Females
I quarter —		
A culicifacies	0	14(*A* 1 *B* 11, *C* 2)
II quarter —		
A culicifacies	0	3(*B* 3)
III quarter	Nil	Nil
IV quarter		
07 00 hour	Nil	Nil

After the hut was sprayed collections were made subsequently for six consecutive nights On these nights collections were *continuously* made from 18 00 to 24 00 hours and all mosquitoes found resting on the walls or roof caught The number of *A culicifacies* and other mosquitoes collected were as follows —

	Males	Females
I quarter —		
A culicifacies	5	68
All others	2	36
II quarter —		
A culicifacies	0	0
All others	0	1

The gonotrophic conditions of females of *A culicifacies* were as follows —

A	*B*	*C*	*D*	*E*	*F*	Total
8	58	2	0	0	0	68

These observations are admittedly limited but strongly suggest that *A culicifacies* do enter D D T sprayed dwellings and take a bloodmeal if facilities for the same are available Most of the mosquitoes collected at night were, however, found dead before the following midday in the cloth cages to which they were transferred, indicating a high rate of mortality In the early morning a few dead mosquitoes were also found on the floor but no numerical observations were possible There were no observations in the outlet window because the door had been kept open

While our huts proved very useful for the study of certain aspects of nocturnal behaviour, they were not quite satisfactory for the completion of the studies after treatment with D D T mainly because man could not be used as a bait The buffalo was satisfactory so far as studies in untreated huts were concerned but was most unsatisfactory for studies after treatment The need now is to find a more ' cooperative ' bait or to find a method of restraining the efficient bait in such a manner that it does not spoil the floor and interfere with studies after treatment

SUMMARY AND CONCLUSIONS

(1) Observations were carried out on the nocturnal behaviour of *A culicifacies* in two experimental huts constructed for the purpose near Poona City from December 1951 *to December 1952 with a break of four months during the monsoon* A buffalo was used as bait for these experiments

(2) When the only available entrance into the hut was a horizontal slit and the door of the hut was closed, fewer mosquitoes entered the hut for the purpose of feeding or shelter than in a similar hut with the door kept fully open

(3) *A culicifacies* enter the dwellings throughout the night but the bulk of the entry takes place before mid night There was some evidence to show that some mosquitoes which enter in the first quarter of the night leave the dwelling and a smaller proportion amongst them re enter subsequently Altogether not more than ten per cent of nocturnal entry for the first time takes place after midnight

(4) Comparing ' ' collections made only from 07 30 to 08 6 per cent of the mosquitoes which ente of the night It is not, however, possible to say whether such egress is towards outdoor shelters or towards another indoor place either for shelter or for feeding In other words these experiments do not throw any light on the degree of endophily in respect of *A culicifacies*

(5) While feeding occurs all through the night and perhaps relatively early after entry, the bulk of the feeding takes place before midnight because the bulk of the entry also takes place before that time

(6) When the door is closed and horizontal slits are provided for entry, there is a greater degree of bar to entry of mosquitoes which do not have an urge for feeding However, even with such obstacles mosquitoes not supposedly in a condition ready for feeding do enter houses during the night On an average about 23 per cent of mosquitoes which enter at night represent those that are not in a condition ready for feeding

(7) About seven per cent of the mosquitoes with fresh blood were found with their ovaries half developed and the previous bloodmeal partially digested As no dissections were made on these mosquitoes it cannot be stated what proportion amongst them represent nulliparous females

(8) About 12 per cent of the mosquitoes which were ready for feeding and which had started feeding showed evidences of interruption This has a great bearing on the extent of malaria transmission as multiple feeding increases the chances of mosquitoes getting infected on the one hand and transmitting infection on the other

(9) Outlet window traps did not prove successful for the study of the behaviour of *A culicifacies*

(10) Preliminary observations made on behaviour of mosquitoes in huts treated with D D T showed that it offered no bar to their entry into treated huts and their taking a bloodmeal There is a very slight evidence of an excito repellant mechanism after contact with treated surfaces but on the whole even those which were excited and repelled have apparently picked up sufficient dose of insecticide to be lethal

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MALARIA CONTROL BY THE USE OF INSECTICIDES

A Global Review.

BY

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(November 3 19 5)

INTRODUCTION

THE advent of insecticides has marked a new stage in the long history of malaria as their application has demonstrated unprecedented success in the control of this disease and the economic feasibility of nation wide control programmes throughout the world Pyrethrum sprays were introduced on a large scale in 1937 followed later in 1945 by the synthetic insecticides The object of this paper is chiefly to review up to date observations made on the use of insecticides in malaria control and particularly their effect on the vector anopheline mosquitoes in different parts of the world * This has helped to point out certain lacunæ in our knowledge in respect of some of the species It is hoped that the review will be of some use as a ready reference to the workers in the field

RATIONALE OF THE METHOD—THEORETICAL CONSIDERATIONS

[illegible] mosquito
[illegible] of a vector
[illegible] t could be
achieved by reducing the number of vector anopheline below a certain figure

*The results in term of malaria control have already been admirably summarized by Simmons and Upholt (19 1) Pampana (19 1) and Russell (195?a)

which was referred to as the critical density of the vector species With the introduction of insecticides, however, a new concept has been put forward that even in the absence of mosquito reduction, malaria reduction can be achieved through interception of the vector A mosquito is able to transmit malaria only ten to twelve days after taking an infected blood feed If this mosquito could be destroyed before the parasite had time to develop to the infective stage, transmission of malaria would not be possible The reduction in the longevity of mosquitoes is achieved through any of the adulticidal methods whether by space or residual *spraying*

Precise [illegible] mosquito would depe[illegible] eated surfaces T[illegible] been grouped as

(*a*) *Indoor biters and indoor resters* which are most associated with man and are consequently the best malaria vectors

(*b*) *Indoor biters and outdoor resters*

(*c*) *Outdoor biters and indoor resters* —Both (*b*) and (*c*) have varying degree of association with man and are consequently malaria vectors of secondary importance

(*d*) *Outdoor biters and outdoor resters* which are the least associated with man and are consequently less important in malaria transmission

It would be obvious that mosquitoes in groups (*a*) and (*b*) have the best *chances of contact with the treated surfaces as they rest or feed indoors, thereby* coming into contact with the treated surfaces In the third group, the mosquitoes may come into contact with the treated surface if they rest in houses after the feed, thus giving a varying degree of malaria control, whereas in the fourth group control by the application of insecticides may not at all be possible

In the first group of mosquitoes reduction or near eradication of the vector *may* result whereas in the other groups, there may or may not be appreciable reduction in mosquito density although malaria control may be achieved through interception of the vector anopheline

These statements are however, oversimplified because whether the species is a zoophilic or anthropophilic and what percentage of the mosquitoes rest indoors or outdoors would affect their control by the application of residual insecticides inside the houses

PRACTICAL RESULTS ACHIEVED

One thing is clear that the application of insecticides has a profound effect on the control of malaria under widely different conditions Malaria reduction to a greater or lesser degree has followed premises spraying with residual insecticides wherever it has been efficiently carried out in spite of the diversified habits of the vector species A good example may be cited of the two most notorious vectors of malaria in India, *A culicifacies* is a domestic species with large numerical prevalence, predominantly zoophilic with poor infectivity rate and on the contrary *A fluviatilis* is a sparse species resting mostly outdoors,predominantly anthropophilic

with high sporozoite rate, yet malaria transmitted by both has been equally well controlled There are, however, a few exceptions where malaria control may be doubtful due to one or the other of the following factors —

(i) *Due to the peculiar habits of the vector species* —The mosquitoes belonging to group (d) mentioned above may not be vulnerable to this method of attack Gabaldon (1953a) has made reference to failure of malaria control with residual insecticides in case of *A bellator* in Trinidad, and also *A minimus flavirostris* in Philippines The malaria transmitted by the former species in Brazil and the latter species in parts of Philippines has, however, been controlled to a certain degree

(ii) *Due to the repellent effect of residual insecticides* —For example *A gambiæ* and *A melas* in Africa are repelled by D D T but are successfully controlled by B H C In the oriental region, Bertram (1951) reported unsuccessful results with D D T on *A minimus* in Assam and Reid (1951) on *A letifer* These findings have not been supported by other workers—Dowling (1951) Hamon and Dufour (1952) as quoted by Gabaldon (1953a) in the case of *A gambiæ* Gilroy (1951) in the case of *A minimus* and Nair (1951) in the case of *A letifer*

(iii) *Due to the development of resistance to residual insecticides* —The development of resistance in vector species may jeopardize control of malaria So far only a few authentic cases of resistance have been reported namely *A sacharovi* in Greece, *A albimanus* in Panama and *A sundaicus* in Indonesia but not to an extent sufficient to interfere very seriously with control programmes

Near eradication of malaria has been reported in the case of *A quadrimaculatus** in U S A , *A darlingi* and *A albimanus* in Venezuela *A fluviatilis* in Bombay State India. On the contrary only slight reduction in malaria has been achieved in the case of following species *A aquasalis* in South America *A vestitipennis* in Mexico *A sacharovi A sergenti* and *A superpictus* in Jordan *A moucheti moucheti* in Belgian Congo, *A albimanus* in Mexico

It would also be obvious from the following pages that uniform results on the same vector species in different areas have not been obtained perhaps due to the varying degree of efficiency with which control programme has been carried out, the differences in the habits of the same species in different areas and other local factors and circumstances

The disparity in the results obtained with different vector species with similar resting and feeding habits is however not clear unless it could be shown that in details the habits were variable Presumably the disparity may be due to the varying proportion of indoor and outdoor resters and biters and whether zoophilic or anthropophilic It would be evident that in case of all the seven species referred to above where only slight reduction of malaria has been reported there are local variations in their resting and feeding habits and food preferences

It may, however, be pointed out that in spite of the fact that insecticides have been used for the control of malaria for about ten years there are a number of species about which no data is available (Table I) It would seem desirable that investigations on these species should be given priority

*Very marked acquired resistance has been reported in the case of *A quadrimaculatus* in certain parts of U S A (Personal communication—K D Quarterman 1955)

TABLE I

LIST OF SPECIES ON WHICH DATA IS NOT AVAILABLE

[illegible]

and *A tessellatus*

The actual results achieved in the field on the effect of insecticides on vector anopheline mosquitoes are briefly summarized in the following pages The data on the resting and feeding habits of mosquitoes and their sphere of influence has also been included *

GROUP (*A*)

INDOOR BITERS AND INDOOR RESTERS

1. *A* (*M*) *aconitus* Donitz, 1902 —Vector in Indonesia and Indo China

Adult females, as a rule, feed and rest indoors They readily feed on man *Anthropophilic indices of 11 2 (caught from houses) and 0 5 (caught from stables)* per cent have been recorded from Indo China and 12 0 (cattle present) and 61 0 (cattle scarce) per cent from Indonesia

In Indonesia, Van Goor *and Lodens (1952) reported reduction in the vector* population and malaria morbidity with D D T residual spray applied at the rate of 200 mg /sq ft

2 *A* (*N*) *albitarsis* Lynch Arribalzaga, 1878 —Vector in Brazil, Columbia and Venezuela

Adults in certain areas may occur in houses and show marked preference for human blood, in other areas they do not appear to occur in houses, and they may have preference for animal blood

In Venezuela, Gabaldon and Berti (1954) have reported malaria eradication Pinotti (1951) in Brazil, reported reduction in malaria morbidity with D D T. residual spray applied at the rate of 200 mg /sq ft though there was no effect on the vector density

3 *A* (*M*) *annularis* Van der Wulp, 1884 —Vector in Eastern India, Pakistan and Burma

Adults are found in large numbers in cattlesheds, and sometimes in houses also Usually they feed and rest indoors They are markedly zoophilic but feed on man as well Anthropophilic indices of 10 0 (cattle present) and 50 0

*Publications by Covell (19?7 1931), Russell *et al* (1943 194? , Boyd (1949) Russell (19 ?b) and Gabaldon (19 ?3b) have been freely consulted

(cattle scarce) per cent have been recorded from Indonesia and 1 6 per cent from Assam, India

In India, Hajra (1948) and Adhikari and Ganguli (1949) recorded reduction in the vector density and malaria morbidity with D D T residual spray applied at the rate of 38-50 mg /sq ft

4 *A (N) aquasalis* Curry, 1932 —Vector in Venezuela, Brazil, Trinidad, Grenada and Santa Lucia

Adults in some localities are anthropophilic and house frequenting and in other zoophilic and sylvan Zoophilic species seldom found in houses when domestic animals are abundant Its vectorial activities may be limited because of this fact

In Brazil, Trinidad, Tobago and Venezuela, Pinnotti (1951) and Gillette (1953) recorded reduction in malaria morbidity with D D T residual spray applied at the rate of 200 mg /sq ft , though there was no effect on the vector density Senior White (1951) has observed in Trinidad that *A aquasalis*, an indoor rester, has been found resting outdoors

5 *A (A) atroparvus* Van Thiel, 1927 —Vector in Baltic, Netherlands, Germany, Portugal, Spain and Rumania

Domestic mosquito, spends most of its life indoors, is powerfully attracted to stabled animals almost to the exclusion of man, but may overflow into human habitations in search of food under various circumstances, among which are disproportionate density of anophelines or scarcity of animals or for other reasons connected possibly with temperature, humidity or odour Although bites man less readily, yet anthropophilic indices 6 09 and 40 0 per cent in Spain and 84 per cent in Holland have been recorded

In Netherlands, Van Thiel (1953) as quoted by Gabaldon (1953*a* 1953*b*), recorded reduction in vector density and malaria morbidity with D D T residual spray applied at the rate of 100-200 mg /sq ft

6 *A (A) aztecus* Hoffman, 1935 —Vector in Mexico

Adults feed indoors as a rule Feed on man or animal without much preference. Rest indoors as well as outdoors

In Mexico, Downs and Bordas (1951) reported reduction in malaria morbidity with D D T residual spray applied at the rate of 200 mg /sq ft

7 *A (A) claviger* —Vector in the Near East, Baku Region, Cyprus and Palestine

A domestic species in Palestine, where it commonly enters houses and freely bites human beings and rests in indoor shelters In some countries it is considered to be wild species and it rarely enters houses

In Greece and Italy, Livadas (1950) and Missiroli *et al* (1948) recorded reduction in malaria morbidity with D D T residual spray applied at the rate of 180-200 mg /sq ft. They did not observe any effect on the vector density

8 *A* (*K*) *cruzi* Dyar and Knab, 1908 —Vector in South East Brazil

Adults feed and rest indoors and outdoors and prefer animal blood

In Brazil, Pinnotti (1951) observed no effect on vector density but there was reduction in malaria morbidity with D D T residual spray applied at the rate of 200 mg /sq ft

9 *A* (*M*) *culicifacies* Giles, 1901 —It is an important vector in India, West Pakistan, Afghanistan, Ceylon and Burma

Adult females feed and rest indoors and they bite man freely but the anthropophilic index is usually low, except during an epidemic Anthropophilic indices of 1 6 and 2 5 per cent have been recorded from India

In India, reduction in vector density and malaria morbidity was recorded by the application of D D T at 50 60 mg /sq ft and of B H C at 10 mg gamma isomer/sq ft (Jaswant Singh and Dalip Singh, 1949, Viswanathan, 1950, Jaswant Singh *et al*, 1951) Similar results were obtained in Pakistan and Ceylon with D D T applications at 25 38 mg /sq ft (Afridi and Bhatia, 1947, Puri and Bhatia, 1947) and 50 200 mg /sq ft (Rajendram and Jayewickreme, 1947) respectively

10 *A* (*N*) *darlingi* Root, 1926 —Vector in British Honduras, Columbia Venezuela, Guianas, Brazil, North West Argentine, Bolivian foot hills, Equador and Peru

This species is markedly anthropophilic, and readily enters houses from dusk to any time at night As a rule, rests in indoor shelters In Venezuela, out of 100 mosquitoes of this species caught 90 to 98 were from human dwellings Anthropophilic index of 63 per cent has been recorded from Brazil

In Brazil, with D D T (200 mg /sq ft) application though there was little effect on vector density, there was reduction in malaria morbidity (Pinnotti, 1951) Similar applications of D D T in Argentina and French Guiana also resulted in reduction in malaria morbidity (Alvarado 1953, as quoted by Gabaldon 1953*a* 1953*b*, and Floch 1952) There was reduction or eradication of the vector as well as malaria in Bolivia (Moscose Carrasco, 1953, as quoted by Gabaldon, 1953*a* 1953*b*) and Columbia (Ranjifo and de Zulueta 1952) and in Venezuela with D D T applications at 200 mg /sq ft

11 *A* (*M*) *farauti* Lavern, 1902 —Vector in Australia, New Guinea, Solomons, Hebrides, New Britain to Eastern Celebes

Adult females may feed and rest indoors or outdoors and take human or cattle blood without much preference

In New Hebrides islands and New Guinea, reduction in vector density and malaria morbidity was recorded with D D T application at the rate of 100 mg /sq ft (Yust, 1947, and Bang *et al*, 1947)

12 *A* (*A*) *freeborni* Aitken, 1939 —Vector in West U S A, and North West Mexico

Adults feed and rest indoors They readily feed on man, show progressively higher prevalence of human, pig, horse and cattle blood in their precipitin tested

stomach contents Malaria has practically disappeared in territories occupied by this vector (Hackett, 1952)

13 *A* (*M*) *funestus funestus* Giles, 1900 —Vector in East, West, Central and South Africa Mauritius and Madagascar

Adult females feed and rest indoors and are anthropophilic It has been shown that the species prefers to bite indoors and that an increase in number of occupants in a hut causes an increase in the number of adult mosquitoes which enter it Anthropophilic index of 61 3 per cent has been recorded in Kenya

Reduction in malaria was observed in Southern Rhodesia (Alves 1951) with B H C (46 mg gamma isomer/sq ft) and in Ruanda Urundi (Jadin, 1951) with D D T (200 mg /sq ft) application Eradication and reduction of the vector and reduction in malaria morbidity has been recorded in Mauritius (D D T 170-260 mg /sq ft.), Reunion and Belgian Congo (D D T 200 mg /sq ft) with D D T applications (Dowling, 1951, Hamon and Dufour 1952 as quoted by Gabaldon 1953*a* 1953*b* and Vincke 1948) There is a very remarkable control scheme in Madagascar, larger than any of the others in which local eradication of this species has been obtained together with *A gambiæ* (Personal communication from Prof G Macdonald, 1954)

14 *A* (*M*) *gambiæ gambiæ* Giles 1900 —Vector in East West Central and South Africa, Mauritius, Madagascar and Reunion

Adult females feed and rest indoors and definitely prefer human blood High anthropophilic indices of about 82 per cent have been recorded from West Africa and Kenya

Jadin (1951) in Ruanda Urundi observed reduction in malaria morbidity with D D T (200 mg / sq ft) application Dowling (1951) in Mauritius (D D T 170-260 mg /sq ft), Hamon and Dufour (1952) as quoted by Gabaldon (1953*a* 1953*b*) in Reunion and Vincke (1948) in Belgian Congo (D D T 200 mg /sq t.) observed that there was no effect on vector density though there was reduction 1 malaria morbidity with insecticidal applications

15 *A* (*M*) *gambiæ melas* Theobald 1903 —Vector in West Africa (coastal ion)

It feeds and rests indoors and prefers human blood

Data on its control by the use of insecticides not available

16 *A* (*M*) *hancocki* Edwards 1929 —Vector in East, West and Central Africa

It feeds and rests indoors and takes human or animal blood without much preference

Data on its control by the use of insecticides not available

17 *A* (*A*) *hyrcanus sinensis* Wiedemann 1928 —Vector in the plains of China and Formosa

It feeds and rests indoors and takes human or cattle blood without much preference In parts of China, it is a voracious human feeder Anthropophilic indices as high as 95 per cent and as low as 0 9 per cent have been recorded from Shanghai and Indo-China, respectively

Reduction in vector density was recorded in Nanking Region, China, with D D T applied at the rate of 150 mg /sq ft (*Agr Res Council Abstracts*, 1950, as quoted by Jaswant Singh *et al*, 1954)

18 *A* (*M*) *Jeyporiensis candidiensis* Koidzumi, 1924 —Vector in Travancore (India), Burma, Indo China and South China

Adult females feed indoors but may rest indoors or outdoors and are strongly anthropophilic Anthropophilic indices of 59 0 and 70 0 per cent have been recorded from Indo China

Data on its control by the use of insecticides not available

19 *A* (*M*) *kochi* Donitz, 1901 —Vector in Indonesia Adults are moderately domestic, frequenting houses and stables and feeding on man and animals

Data on its control by the use of insecticides not available

20 *A* (*A*) *labranchiæ* Falleroni, 1926 —Vector in Spain, Morocco, Algeria, Tunisia, Italy, Corsica, Sardinia and Sicily

Adult females enter houses in large numbers They are not known anywhere to be effectively deviated from man by domestic animals They prefer to feed, rest and hibernate in buildings This makes house spraying with insecticides specially effective

In Italy Missiroli *et al* (1948) reported reduction in vector density and malaria morbidity with D D T (200 mg /sq ft) residual spray

21 *A* (*A*) *maculipennis maculipennis* Meigen, 1818 —Vector in Turkey and Bulgaria

Adult females feed and rest indoors and outdoors and prefer animal blood but at times may feed on man

Livadas (1950) recorded reduction and eradication of vector and reduction in malaria morbidity in Greece with D D T (180 mg /sq ft) residual spray Missiroli *et al* (1948) in Italy observed reduction in malaria morbidity but little effect on vector density with D D T applied at the rate of 200 mg /sq ft

22 *A* (*M*) *mangynus* Banks 1906 —Vector in Philippines

It bites indoors but may rest indoors or outdoors

In Philippines Bhatia (1953) as quoted by Jaswant Singh *et al* (1954) recorded reduction in its density with D D T applied at the rate of 200 mg /sq ft

23 *A* (*A*) *messae* Falleroni 1926 —Vector in Hungary, Germany, Poland U S S R, Balkans and Manchuria

It is powerfully attracted to stabled animals almost to the exclusion of man, but may overflow into human habitation in search of food under various circumstances among which are a disproportionate density of anophelines or scarcity of animals, or for other reasons connected possibly with temperature, humidity or odour Anthropophilic index of 63 0 per cent has been recorded in Holland

In Netherlands, Cseh Firtos (1952) recorded reduction in vector density and malaria morbidity with D D T residual spray applied at the rate of 200 300 mg /sq ft

24 *A (M) minimus minimus*—Vector in North east India Burma, Indo-China South China, Formosa, Indonesia, Hong Kong, Thailand, Amoy Island, Sumatra, Celebes and Moluccas

Mainly a domestic species with a high preference for human blood It feeds indoors but may rest indoors or outdoors Anthropophilic indices as high as 85 7 and 92 4 per cent have been recorded from India

In India, D D T applied at the rate of 50 120 mg /sq ft (Puri and Krishnaswami, 1947, Kar, 1950, and Krishnaswami 1952) and in Thailand at ..0 mg /sq ft (Bhatia, 1953, as quoted by Jaswant Singh *et al*, 1954) resulted in reduction of vector density and malaria morbidity

25 *A (M) moucheti moucheti* Evans 1925—Vector in Belgian Congo and Uganda

It feeds and rests indoors and takes human or animal blood without much preference

Davidson (1950) as quoted by Gabaldon (1953*a* 1953*b*) recorded slight reduction in malaria morbidity with B H C applied at the rate of 10 mg gamma isomer/sq ft

26 *A (M) moucheti nigeriensis* Evans 1931—Vector in Nigeria

It feeds and rests indoors and takes human or animal blood without much preference Data on its control by the use of insecticides not available

27 *A (M) nili* Theobald, 1901—Vector in Belgian Congo Liberia, Sierra Leone

In some parts, this species enters houses bites man and may be an important vector of malaria, whereas in others the insect is rare and is of no importance

Data on its control by the use of insecticides not available

28 *A (M) philippinensis* Ludlow, 1902—Vector in Bengal India and East Pakistan

Adults chiefly rest in houses usually 1½ ft off the floor, biting at night between 8 p m and 4 a m In Assam this species appears to be zoophilic An anthropophilic index of 6 4 per cent has been recorded from Assam, India

In East Pakistan, Nasir ud din (1952) recorded reduction in malaria morbidity with D D T applied at the rate of 106 mg /sq ft

29 *A (A) pseudopunctipennis* Theobald 1901—Vector in Mexico, Columbia, Bolivia Peru Chile, Argentina probably Gautemala, Venezuela and Equador

As a rule, adult females feed and rest indoors and take human or animal blood without much preference Anthropophilic indices of 50 to 67 6 per cent in Argentina and 2 5 per cent in Venezuela have been recorded

In Mexico, Downs *et al* (1950) observed reduction in vector density and malaria morbidity with D D T application (200 mg /sq ft) Similarly D D T (200 mg /sq ft) residual spray in Columbia Ecuador, Peru (Montalvan, 1953) and Argentina (Alvarado, 1953 as quoted by Gabaldon, 1953*a* 1953*b*) resulted

in the reduction of malaria morbidity In Bolivia and Venezuela, D D T. applied at the rate of 200 mg /sq ft reduced malaria morbidity but had little effect on vector density (Downs *et al*, 1950 and Moscoso-Carrasco, 1953, as quoted by Gabaldon, 1953*a* 1953*b*)

30 *A* (*M*) *pulcherrimus* Theobald, 1902 —Vector in Caucasus and Iraq

The females of this species like to concentrate around settlements, but they occur also far from man and his herds As resting places, they choose buildings as well as outdoor places, burrows, vegetation and the like They viciously bite man and animals It is a bold feeder attacking animals and man in the open by day or by night

Data on its control by the use of insecticides not available

31 *A* (*M*) *punctulatus* Donitz, 1901 —Vector in New Guinea, Solomons to Halmahera

Adult females feed and rest indoors or outdoors and take human or cattle blood without much preference

Data on its control by the use of insecticides not available

32 *A* (*A*) *quadrimaculatus* Say, 1924 —Vector in Central, South and East U S A

Adults are most active at night, females fly as far as one mile to obtain animal or human blood meal, and readily enter houses where they often spend daylight *hours in dark corners It is the most abundant anopheline found in houses and* other man-made shelters, prefers bovine hosts, but at times or in places feeds on man

Andrews (1951) recorded reduction in vector density and malaria morbidity in U S A, with D D T residual sprays (200 mg /sq ft)

33 *A* (*M*) *rufipes* Gough, 1910 —Vector in West Africa, coastal region

Adults have been found in human dwellings, cowsheds, and outdoor haunts including rock clefts and cavities in banks along streams

Data on its control by the use of insecticides not available

34 *A* (*A*) *sacharovi* Favre, 1903 —It is an important vector in Balkans, Near East, Central Russia and West China

Adults enter human habitations where they persistently bite man They sometimes feed indiscriminately on man and domestic animals and rest indoors or outdoors

Reduction or eradication of the vector species and reduction in malaria morbidity has been recorded from Greece (D D T 100 mg /sq ft) (Livadas, 1950), Italy (D D T 200 mg /sq ft) (Missiroli *et al*, 1948) and Jordan (D D T 200 mg / sq ft) (Farid, 1953) with D D T residual sprays

35 *A* (*M*) *sergenti* Theobald, 1907 —Vector in Canary Islands, Egyptian oases, Transjordan and Israel

Adults readily enter houses, and bite most frequently after dark, prefer animal blood but at times bite man They are found resting in caves, karezes, also in houses and tents

In Jordan, Farid (1953) observed slight reduction in malaria morbidity but little effect on vector density with D D T applied at the rate of 200 mg /sq ft.

36 *A (M) stephensi mysorensis* Sweet and Rao, 1937 —Vector in South India Considered less important as vector than the type form, but Senior White as quoted by Boyd (1949) considered it to be chief rural carrier in Vizagapatam (India)

This species is less hardy than the type form and has more zoophilic tendencies

Data on its control by the use of insecticides not available

37 *A (M) stephensi stephensi* Lisbon, 1901 —Vector in Persian Gulf area and India

It feeds and rests indoors Adults are commonly found in houses, barracks and cowsheds Feeds avidly on man

In West Pakistan, Afridi and Bhatia (1947) recorded reduction in vector density and malaria morbidity with D D T sprayed at the rate of 25 38 mg /sq ft In India similar results were achieved by Adhikari and Ganguli (1949) with D D T applications (100 mg /sq ft)

38 *A (M) subpictus subpictus* Grassi, 1899 —Vector in Celebes

It feeds indoor but may rest indoors or outdoors Adults are found in large numbers in houses and in cattlesheds They may feed on man but apparently prefer cattle Anthropophilic indices as low as zero and as high as 25 0 per cent have been recorded from India

Data on its control by the use of insecticides not available

39 *A (M) sundaicus* Rodenwaldt, 1926 —Vector in North east India, East Pakistan, Indonesia, Andaman Malaya, Sarawak and Borneo

They rest in houses and cowsheds and are voracious feeders biting by day as well as by night They may bite indoors or outdoors In Indonesia it shows an overwhelming preference for human blood even in the presence of cattle Anthropophilic indices of 94 0 and 86 0 per cent have been recorded from Indonesia

In India (D D T 100 mg /sq ft) and Indonesia (D D T 200 mg /sq ft) reduction in vector density and malaria morbidity was recorded with D D T residual sprays (Adhikari and Ganguli, 1949 and Van Thiel and Winoto, 1951)

40 *A (M) superpictus* Grassi, 1899 —Vector in Eastern Mediterranean countries including southern Italy, Near East, U S S R , and Baluchistan (Pakistan)

Adults readily enter houses, tents and barracks, and females prefer human blood They are found in large numbers in outside resting places also (caves and karezes) Anthropophilic indices of 48 1, 29 7, and 23 3 per cent of those captured in stables were recorded from Yugoslavia, Greece and Cyprus, respectively

In Greece, (D D T 180 mg /sq ft), Pakistan (D D T 25 50 mg /sq ft) and Afghanistan with D D T residual sprays (D D T 112 200 mg per sq ft) reduction in vector density and malaria morbidity was recorded (Livadas, 1950, Afridi and Bhatia, 1947, Puri and Bhatia, 1947, and Rao, 1951)

41 *A* (*M*) *varuna* Iyengar, 1924—Vector of local importance in some hilly and foot hill areas of East Central India

The adults are found both in cowsheds and human habitations, and feed readily on man

Senior White (1945) obtained effective control of this species for eight weeks in Jeypore hill tracts, India, with D D T applied at the rate of 50 mg /sq ft

42 *A* (*A*) *vestitipennis* Dyar and Knab, 1906—Vector in Mexico and British Honduras

Adult females readily enter houses and feed indoors but may rest in indoor or outdoor shelters They take human or animal blood without much preference

In Mexico with D D T applied at the rate of 200 250 mg per sq ft, Salinas Dopez and Roquet Perez (1950) obtained slight reduction in malaria morbidity but no effect on vector density

GROUP (*B*)

Indoor biters and outdoor resters

1 *A* (*N*) *albimanus* Wiedemann, 1921—Vector in Central America, West Indies Caribbean Coast, Venezuela, Columbia, Pacific Coast and Ecuador

It feeds indoors but rests in outdoor shelters Adults are nocturnal in habits and avid feeders on man who may be the preferred host, or on horses, cows, goats or pigs They invade houses in large numbers but do not, as a rule, remain in houses after sunrise Its domesticity is low in Venezuela Out of 100 mosquitoes of this species caught, two to five come from houses Anthropophilic index of 34 per cent has been recorded in Venezuela

With D D T residual sprays, reduction in vector density and malaria morbidity has been recorded in Puerto Rico (D D T 150 200 mg /sq ft) (Gahan and Lindquist, 1945), Ecuador (D D T 150 200 mg /sq ft) (Montalvan 1953) Venezuela (D D T 200 mg /sq ft) (Gabaldon, 1953*a* 1953*b*) and Panama (D D T 200 mg /sq ft) (Galindo and Gallardo, 1947 as quoted by Gabaldon, 1953*a* 1953*b*) In Mexico there was slight reduction in malaria morbidity but little effect on vector density with D D T applied at the rate of 200 250 mg /sq ft

2 *A* (*M*) *fluviatilis* James, 1902—Vector in hill and foot hill regions of India

They feed indoors and a significant fraction of population is in outdoor resting places during the day The species seems to be composed of two biological races, one is strongly anthropophilic, while the other feeds almost exclusively on cattle Anthropophilic indices as high as 87 0 per cent and as low as 1 0 per cent have been recorded in India

With D D T residual sprays (50 60 mg /sq ft) reduction in vector density and malaria morbidity has been recorded in India (Ramakrishnan *et al*, 1948, Vedamanikkam, 1949, Jaswant Singh and Kariappa, 1949, Viswanathan, 1950, and Srivastava and Chakrabarti, 1952)

3 *A* (*M*) *letifer* Gater, 1941, Sandosham, 1945—Vector in Malaya

Adults are found in deeply shaded places in jungle and also in houses It s indoors and outdoors but rests in outdoor shelters It has marked preference human blood and seldom attacks cattle (Nair, 1947*a*)

With D D T application at the rate of 100 mg /sq ft, Nair (1947*b* 1951) rded reduction in vector density and malaria morbidity

4 *A* (*M*) *leucosphyrus leucosphyrus* Donitz, 1901—Vector in North east im (India), Borneo, Indonesia and Burma

Adults are wild and naturally occur in dense jungle, but may be found in ses also It feeds indoors but rests outdoors Adults appear to take human nimal blood without much preference Anthropophilic index of 75 5 per cent been recorded in India

Data on its control by the use of insecticides not available

5 *A* (*M*) *maculatus maculatus* Theobald, 1901—Vectors in Malaya, onesia, Yunnan and Hong Kong

Adults enter houses readily, bite man between 9 p m and 2 a m and during day are found in houses, cattlesheds and outdoor resting places Apparently feeding habits of this species differ in different parts In Assam Indo China, th China and Philippines it appears to be zoophilic while in Malaya and onesia it is anthropophilic Anthropophilic indices as high as 97 0 and low as 2 8 per cent have been recorded in Indonesia and Philippines, ectively

Schiphorst (1952) (as quoted by Gabaldon 1953*a* 1953*b*), obtained reduction nalaria morbidity with D D T residual application (200 mg /sq ft) whereas llace (1948) recorded reduction in vector density with little effect on malaria bidity with D D T applied at the rate of 100 mg /sq ft

6 *A* (*M*) *minimus flavirostris* Ludlow 1914—Vector in Philippines, neo, Java and Celebes

It bites indoors but rests in outdoor shelters Adults bite man and cattle out much discrimination They enter houses at night to feed but do not rest le During the day, they frequently rest under overhanging stream banks

In Philippines Smith and Dy (1949) obtained little effect on vector density D D T applied at the rate of 200 mg per sq ft Bhatia (1953) (as quoted by vant Singh *et al*, 1954) recorded reduction in vector density and malaria bidity with D D T residual spray applied at the rate of 200 mg per sq ft

7 *A* (*A*) *novumbrosus* Strickland, 1916—Vector in Malaya

It may feed indoors or outdoors but it rests in outdoor shelters There is fficient evidence regarding its preference for human or cattle blood

Data on its control by the use of insecticides not available

8 *A* (*M*) *pharoensis* Theobald, 1901—Vector in Egyptian delta and oases Uganda Congo

It feeds indoors but rests in outdoor shelters It may be strongly (South eria) or weakly (Kenya) anthropophilic In Egypt, anthropophilic index of

those caught from houses and tents was 97 5 per cent and those from stables 10 8 per cent Apparently spends the day in ricefields as none are found in stables, houses or similar shelters (Nile Valley) Prof G Macdonald s experience is very much against this observation (personal communication, 1954)

Data on its control by the use of insecticides not available

9 *A* (*A*) *punctimaculatus* Dyar and Knab, 1906 —Vector in Columbia, Peru and Panama

It feeds and rests indoors and outdoors and prefers cattle blood Adults are abundant in undrained jungle areas and the females engage in flights, invade dwellings and feed on human blood

Data on its control by the use of insecticides not available

10 *A* (*A*) *umbrosus* Theobald, 1903 —Vector in Malaya and Indonesia

It feeds indoors or outdoors but rests outdoors Adults are fierce biters and are found in deeply shaded places in dense forests and also in houses They have marked preference for human blood Anthropophilic index of 95 0 per cent has been recorded from Malaya

Data on its control by the use of insecticides not available

GROUPS (*C*) AND (*D*)

OUTDOOR BITERS AND INDOOR RESTERS , OUTDOOR BITERS AND OUTDOOR RESTERS

1 *A* (*A*) *bancrofti bancrofti* Giles, 1902 —Vector in Australia and Dutch New Guinea

Adults rarely frequent houses It is said to vary a great deal in its feeding habits in different areas In South Queensland it attacks human beings in the bush in the daytime while at Cairns it is said to show some definite discrimination against man

Data on its control by the use of insecticides not available

2 *A* (*A*) *barbirostris* Vander Wulp, 1884 —Vector in Malaya and Indonesia

To a large extent this is a wild species It is more frequently found in houses in the Indian areas than further east It is the common species in houses in Celebes The form occurring in India seems to prefer blood of domestic animals, but in Celebes this species is apparently anthropophilic Anthropophilic index of 9 0 (cattle present) and 31 0 (cattle scarce) per cent have been recorded from Indonesia and 95 per cent from Malaya

Data on its control by the use of insecticides not available

3 *A* (*K*) *bellator* Dyar and Knab, 1906 —Vector in Brazil and Trinidad

It may feed indoors or outdoors but rests in outdoor shelters In Trinidad it does not enter houses in numbers and transmission of malaria is undoubtedly almost entirely out of doors It prefers animal blood but may feed on man

In Brazil, Pinotti (1951) recorded reduction in malaria morbidity but little effect on vector density with D D T applied at the rate of 200 mg /sq ft

4 A (M) *hargreavesi* Evans, 1927 —Vector in West Africa inland

It feeds outdoors but may rest in indoor or outdoor shelters Takes human or animal blood without much preference

Data on its control by the use of insecticides not available

5 A (A) *hyrcanus nigerrimus* Giles, 1900 —Vector in Indo-China, Malaya and Indonesia

Adults are rarely found in houses but are found more often in cattlesheds They feed and rest outdoors They bite man outside in the evening and even in the shade during the day This is considered to be a zoophilic species Anthropophilic indices of 83 0, 30 2, and 3 8 per cent have been recorded from Indonesia Malaya and India, respectively

Data on its control by the use of insecticides not available

6 A (A) *hyrcanus williamsoni* Baisas and Hu, 1936 —Vector in Java and Celebes

It feeds and rests indoors or outdoors There is insufficient evidence regarding its preference for human or cattle blood

Data on its control by the use of insecticides not available

7 A (N) *nuneztovari* Gabaldon, 1940 —Vector in Venezuela

Authentic data on its habits not available

Gabaldon (1953a 1953b) with D D T application (200 mg /sq ft) in Venezuela, obtained slight reduction in malaria morbidity but little effect on vector density

8 A (M) *tessellatus* Theobald, 1901 —Vector in Maldiv islands

Adults are found resting among trees in the jungle along banks of streams, but have been taken also in houses and cowsheds

Data on its control by the use of insecticides not available

SUMMARY

The observations on malaria control *vis-a vis* the application of insecticides has been reviewed from the global standpoint

(a) Use of residual insecticides has resulted in effective control of malaria transmitted by the following vector species

A aconitus, *A albitarsis*, *A annularis* *A aquasalis*, *A atroparvus*, *A aztecus*, *A claviger* *A cruzi*, *A culicifacies*, *A darlingi*, *A farauti*, *A freeborni*, *A funestus funestus*, *A gambiae gambiae*, *A hyrcanus sinensis* *A labranchiae*, *A maculipennis maculipennis*, *A mangyinus*, *A messeae*, *A philippinensis*, *A pseudopunctipennis*, *A quadrimaculatus*, *A sacharovi*, *A stephensi stephensi*, *A sundaicus*, *A albimanus*, *A fluviatilis*, *A letifer*, *A maculatus maculatus* and *A minimus minimus*

(b) In some countries, use of residual insecticides has not resulted in effective control of malaria in respect of the following vector species due to the various factors outlined

A bellator, *A nuneztovari*, *A minimus flavirostris*, *A moucheti moucheti*, *A sergenti*, *A vestitipennis* and *A maculatus maculatus*

(*c*) It may, however, be pointed out that in spite of the fact that insecticides have been used for the control of malaria for about ten years there are a number of species listed below about which no data is available

A pulcherrimus, *A gambiæ melas*, *A hancocki*, *A hargreavesi*, *A moucheti nigeriensis*, *A pharoensis*, *A rufipes*, *A barbirostris*, *A hyrcanus nigerrimus*, *A jeyporiensis candidiensis*, *A leucosphyrus leucosphyrus*, *A novumbrosus*, *A stephensi mysorensis*, *A subpictus subpictus*, *A umbrosus*, *A bancrofti bancrofti*, *A punctulatus*, *A kochi*, *A punctimaculatus*, *A brunnipes*, *A funestus imerinensis*, *A nili*, *A hyrcanus williamsoni*, *A ludlowi torakala* and *A tessellatus*

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Indian Journal of Malariology, 9, 4, December 1955

INDEX OF AUTHORS.

Page

N

P

Page

R

S

V

INDEX OF SUBJECTS

RECORDS OF THE MALARIA SURVEY OF INDIA.

Vol I No 1 (October 1929)	A Bibliography of Malaria in India	Sinton
Vol I No 2 (March 1930)	Collected Memoranda on Malaria 1847 1924	
Vol I, No 3 (October 1930)	Malaria in Peshawar Malaria in Delhi Note on Malaria in Delhi Malaria in Sind Notes on Malaria in Sind Canal Irrigation and Malaria Rice Cultivation and Malaria	Richmond and Mendis Senior White Sinton Young and Majid Sinton Gill Gill
Vol I, No 4 (December 1930)	Experiments on the Value of Cinchona Alkaloids Relative Values of Cinchona Alkaloids Malaria in Madras Presidency Spleen Rates in the Garo Hills Paris Green as a Larvicide Malaria in Sind Parts I to III	Sinton Sinton Rao Shortt Chalam Covell and Baily
Vol II No 1 (March 1931)	[illegible]	Covell Clyde Macdonald and Chowdhury Barraud Christophers and Barraud
Vol II No 2 (June 1931)	Mosquito Survey at Birnagar [illegible]	Bose Covell Barraud and Christophers Sinton and Kehar Christophers Butt
Vol II, No 3 (September 1931)	[illegible] III	Schuffner Sinton Chowdhury Macdonald and Majid Christophers and Puri Mulligan
Vol II No 4 (December 1931)	Malaria in Sind Parts IV to VII Splenomegaly in Malarious Communities Malaria in Bikaner Malaria in Peshawar *A gambiae* in Seychelles Dissections of Anophelines in Mysore	Covell and Baily Macdonald Macdonald Richmond Hermitte Sweet and Rao
Vol III No 1 June 1932)	Malaria in Calcutta Malaria in Patiala State Malaria in Sind Part VIII Anti Malarial Measures in Sylhet Assam Malaria in Tea Estates in Sibsagar District Assam *A philippinensis* as a Carrier in Bengal Wire Gauze Screens Spectra Studies in Malarial Sera	Covell Covell Covell and Baily Strickland and Murphy Manson and Ramsay Bose Mulligan and Majid Kehar

Vol III, No 2 (December 1932)		ABRAHAM
		SARKAR
		RAMSAY AND CARPENTER
		RICE AND SAVAGE
		GUPTA *et al*
		PUNJAB WATERLOGGING BD
		COVELL
		COVELL AND BAILY
	Studies in Malarial Immunity Part I	SINTON AND MULLIGAN
	Helminthic Infections in Anophelines	SINTON
	A aitkeni James var *N pinjaurensis*	BARRAUD
	Identification of Monkey Malaria Parasites Pt I	SINTON AND MULLIGAN
Vol III, No 3 (June 1933)		SINTON AND MULLIGAN
		KARAMCHANDANI
		MAJID
		MANSON AND RAMSAY
		SINTON
		BARRAUD
		BARRAUD
	Studies in Malarial Immunity Part II	MULLIGAN AND SINTON
	Malaria in Kalimpong and Sikkim	SUR, BHATTACHARJI & KHAN
	Malaria Survey in Patna	BASU
	Mosquitoes and Sandflies in Rajputana	JASWANT SINGH
Vol III, No 4 (December 1933)	Malaria and Waterlogging	LAL AND SHAH
	Malaria in Mysore State Parts I to III	SWEET
		SWEET AND RAO
	. II	SINTON AND MULLIGAN
		MULLIGAN AND SINTON
		NEAL AND SAVAGE
		GUPTA *et al*
Vol IV, No 1 (March 1934)		SINTON
		SINTON AND GHOSH
	II	GHOSH AND SINTON
		IYENGAR
		MEHTA
Vol IV, No 2 (June 1934)		SENIOR WHITE AND ADHIKARI
		SWEET AND RAO
		SWEET
		COVELL AND BAILY
		SATYANARAYANA
	Larvæ	MANSON
		SINTON AND GHOSH
Vol IV, No 3 (September 1934)	Studies in Untreated Malaria	LOWE
	Notes on Malaria in Mysore State Part VII	NURSING, RAO AND SWEET
		BOSE
	art I	MEHTA
		COVELL
		KNOWLES AND BASU
		GHOSH AND NATH
		COVELL AND BAILY
Vol IV, No 4 (December 1934)		SATYANARAYANA
		MEASHAM AND CHOWDHURY
		WATS AND GHOSH
		IYENGAR
	'fonkey	KHAZAN CHAND AND HARBHAGWAN
		SINTON
		MEHTA

Vol V, No 1 (March 1935)	A Method for Cleaning the Capillary Tubes	Sinton
	Dispersion of Anopheline Larvæ	Sinton and Mason
	Taxonomy of *A maculipennis*	Karamchandani
	Effect of Atmospheric Humidity on *C fatigans*	Karamchandani
	Clinical Efficacy of Totaquina	Hicks and Diwan Chand
	Malaria on the Barsi Light Railway (Deccan)	Lindberg
Vol V, No 2 (June 1935)	Anopheles Breeding and Rice Cultivation	Sen
	Malaria in Sind Parts XIII and XIV	Covell and Baily
	Experiment with Paris Green in Sind	Covell, Baily and Prasad
	Paris Green Dusting on Rice Crops	Covell
	The Emergence of Anophelines	Sen
	Changes in the Proteins of the Blood Sera	Ghosh and Sinton
	Atebrin Musonate	Hicks
Vol V, No 3 (September 1935)	[illegible]	Sen
	[illegible]	Sen
	[illegible]	Ganguli
	[illegible]	Sinton
	[illegible]	Puri
	[illegible]	Sinton and Wats
	[illegible]	Sinton and Harbhagwan
	[illegible]	Gupta *et al*
	[illegible]	Gupta *et al*
	[illegible]	Mulligan
Vol V, No 4 (December 1935)	[illegible]	Timbres
	[illegible]	Rice
	[illegible]	Pandit
	[illegible]	Kehar
	[illegible]	Sinton
	[illegible]	Dempster
	[illegible]	Singh and Harbhagwan
	[illegible]	Rice
	[illegible]	Sinton
Vol VI, No 1 (March 1936)	Cholesterol Changes in Malaria	Krishnan *et al*
	Malaria Control by Subsoil Drainage	Senior White
	Tebetren in Malaria	Manson
	Larva of *Anopheles gigas* var *baileri*	Rice *et al*
	Bionomics of *Anopheles sundaicus*	Neogi
	Androphilic Indices of certain Anophelines	Ramsay *et al*
	Malaria Food Supply and Population in India	Sinton
	Anopheles habibi from Quetta	Mulligan and Puri
	Aedes egypti in Aeroplanes	Hicks and Diwan Chand
	What Malaria Costs India (*contd*)	Sinton
Vol VI, No 2 (June 1936)	Atebrin and Atebrin Musonate in Malaria	Seelig and Wadhawa Singh
	[illegible]	Puri
	[illegible]	Lampbell
	[illegible]	Neogi
	[illegible]	Viswanathan
	[illegible]	Molony and Gorman
	[illegible]	Mulligan and Baily

Vol VI, No 3 (September 1936)		COVELL AND BAILY
		COVELL AND BAILY
		SENIOR WHITE
		RAO AND CHELUVARAYAN
		DIKSHIT
		CHOWDHURY
		PAUL, DAS AND ROY
		KEHAR
		KEHAR
		A CORRECTION
		A CORRECTION
Vol VI, No 4 (December 1936)	Mosquito Survey of Karachi Air Port	HICKS AND DIWAN CHAND
	Gambusia affinis under Indian Conditions	MULLIGAN AND MAJID
	'Entoray' Machine Experiments	WATS AND BILDERBECK
	A minimus in Assam	RICE AND MOHAN
	Mosquito Catching Machine Experiments	SENIOR WHITE *et al*
	Larvivorous Fishes of India	PRASHAD AND HORA
	Mosquito Control Work in Vizagapatam Port	EBDEN AND SATYANARAYANA
Vol VII, No 1 (March 1937)		HICKS AND MAJID
		SENIOR WHITE
		DIKSHIT
		SINTON
		COVELL AND AFRIDI
		MAJID
		WATS AND SINGH
		A CORRECTION
Vol VII, Nos 2 and 3 (June September 1937)		KEHAR
		KEHAR AND HARBHAGWAN
		SEN
		SENIOR WHITE
		WATS AND HARBHAGWAN
		RAO AND SWEET
		SWEET
		GORE
		NEOGI AND KHAN
Vol VII, No 4 (December 1937)		SENIOR WHITE AND ADHIKARI
		RUSSELL
		GIDEON *et al*
		SHORTT AND MENON
		GREWAL

JOURNAL OF THE MALARIA INSTITUTE OF INDIA.

Vol III, No 4 (December 1940)	Senior White and Adhikari
	Senior White & Narayana
	Russell and Rao
	Passmore and Sommerville
	Chopra *et al*
	Mondal
	Nandi
	Chopra *et al*
	Roy
	Rao and Ramakrishna
	Mulligan *et al*
	Dikshit and Ganapathi
	Russell and Knipe
	Russell and Rao
	Mulligan *et al*
	Mulligan *et al*
	Mulligan *et al*
	Mulligan and Swaminath
Vol IV, No 1 (June 1941)	Covell
	Russell *et al*
	Mulligan *et al*
	Viswanathan
	Senior White
	Thomson
	Clark and Choudhury
	Chopra *et al*
	Sen
	Viswanathan
	James
Vol IV, No 2 (December 1941)	Sivalingam and Rustomjee
	Shortt *et al*
	Iyer *et al*
	Russell and Knipe
	Dikshit
	Menon
	Job
	Thomson
	Thomson
	Sen
	Russell and Rao
	Viswanathan *et al*
	Rao
Vol IV, No 3 (June 1942)	Russell *et al*
	Russell *et al*
	Rao and Ramoo
	Russell and Jacob
	Viswanathan
	Venkat Rao *et al*
	Rao and Ramoo
	Roy and Biswas
	Khan
[illegible]	Panigrahi

Vol IV, No 4 (December 1942)	New Variety of *A turkhudi* from Palestine	SALITERNIK AND THEODOR
	[illegible]	IYENGAR
		DE BURCA AND YUSAF
		WIJESUNDARA
		COVELL AND PRITAM SINGH
		THOMSON
		THOMSON
		RUSSELL AND KNIPE
		RAO AND RAMOO
Vol V, No 1 (June 1943)	Studies on Infectivity of *A stephensi*	KNOWLES AND BASU
	Studies on Infectivity of *A annularis*	BASU
	Breeding places of *A fluviatilis*	ADISUBRAMANIAM AND VEDAMANIKKAM
	[illegible]	RUSSELL *et al*
		RAJINDAR PAL
		COVELL AND JASWANT SINGH
		SUNDARESAN AND RAO
		SUBBARAMAN AND VEDAMANIKKAM
	A subpictus as a Malaria Carrier	ROY
	Breeding of *A stephensi* in Salt Water	BASA
	Malaria Control at Pattukkottai	RAO
	Malaria in Ahmedabad	JASWANT SINGH AND JACOB
Vol V, No 2 (December 1943)	[illegible] of Malaria in War	COVELL
		SENIOR WHITE *et al*
		SENIOR WHITE AND RAO
		SENIOR WHITE
		DE BURCA
		DE BURCA AND SHAH
		RAJINDAR PAL
		RAJINDAR PAL
		VISWANATHAN AND RAO
		SIVALINGAM
Vol V, No 3 (June 1944)	[illegible]	JASWANT SINGH AND JACOB
		ABRAHAM AND SAMUELS
		YACOB AND SATYA SWAROOP
		D ABRERA
		SIDDONS
		SIDDONS
		MENON
		BIRD
		SAMARASINGHE *et al*
Vol V, No 4 (December 1944)	Anopheles of India and the Far East	COVELL
	Malaria Control in Deltaic Bengal	IYENGAR
	Behaviour of *A fluviatilis* Part II	VISWANATHAN *et al*
	Mineral Oil as Larvicide	JAYEWICKREME
	Epidemiology of Malaria in Ceylon	RUSTOMJEE
	Malaria in Jharia Mining Settlement	RAO
Vol VI, No 1 (June 1945)	Infant Malaria in North Kanara	VISWANATHAN
	Periodicity of Malaria Epidemics	*YACOB AND SWAROOP*
	Bionomics of *A culicifacies* Part II	RAJINDAR PAL
	Laboratory Colony of *A fluviatilis*	MOHAN
	Behaviour of *A fluviatilis* Part III	RAO
	Spray killing with DDT and Pyrethrum	SENIOR WHITE
	Malaria in Vizagapatam	SUBBARAO AND APPARAO
	Malaria in Salsette Island	VISWANATHAN
	Malaria in Pandharpur	SOMAN

Vol IV, No 4 (December 1942)	New Variety of *A turkhudi* from Palestine	Saliternik and Theodor
	Malaria in the Deltaic Region of Bengal	Iyengar
	New Variation of *A gambiæ*	de Burca and Yusaf
	Mosquitoes of Rat holes in Trees, etc, in Ceylon	Wijesundara
	Malaria in the Coastal Belt of Orissa	Covell and Pritam Singh
	Behaviour of *A minimus* Part VII	Thomson
	Behaviour of *A minimus* Part VIII	Thomson
	Control of Rural Irrigation Malaria	Russell and Knipe
	Control of Mosquito Breeding by Fish	Rao and Ramoo
Vol V, No 1 (June 1943)	Studies on Infectivity of *A stephensi*	Knowles and Basu
	Studies on Infectivity of *A annularis*	Basu
	Breeding places of *A fluviatilis*	Adisubramaniam and Vedamanikkam
	[illegible] Part IV	Russell *et al*
	[illegible]	Rajindar Pal
	[illegible]	Covell and Jaswant Singh
	[illegible]	Sundaresan and Rao
	[illegible]	Subbaraman and Vedamanikkam
	A subpictus as a Malaria Carrier	Roy
	Breeding of *A stephensi* in Salt Water	Bana
	Malaria Control at Pattukkottai	Rao
	Malaria in Ahmedabad	Jaswant Singh and Jacob
Vol V, No 2 (December 1943)	[illegible] Treatment of Malaria in War	Covell
	[illegible]	Senior White *et al*
	[illegible]	Senior White and Rao
	[illegible]	Senior White
	[illegible]	de Burca
	Anopheles from Eritrea	de Burca and Shah
	Histological Structure of Midgut	Rajindar Pal
	Longevity of *A fluviatilis*	Rajindar Pal
	Behaviour of *A fluviatilis* Part I	Viswanathan and Rao
	Spleen and Parasite Surveys in Ceylon	Sivalingam
Vol V, No 3 (June 1944)	[illegible]	Jaswant Singh and Jacob
	[illegible]	Abraham and Samuels
	[illegible]	Yacob and Satya Swaroop
	[illegible]	D Abrera
	[illegible]	Siddons
	[illegible]	Siddons
	[illegible]	Menon
	[illegible]	Bird
	[illegible]	Samarasinghe *et al*
Vol V, No 4 (December 1944)	Anopheles of India and the Far East	Covell
	Malaria Control in Deltaic Bengal	Iyengar
	Behaviour of *A fluviatilis* Part II	Viswanathan *et al*
	Mineral Oil as Larvicide	Jayewickreme
	Epidemiology of Malaria in Ceylon	Rustomjee
	Malaria in Jharia Mining Settlement	Rao
Vol VI, No 1 (June 1945)	[illegible] Malaria in North Kanara	Viswanathan
	[illegible]	Yacob and Swaroop
	[illegible]	Rajindar Pal
	[illegible]	Mohan
	[illegible]	Rao
	[illegible]	Senior White
	Malaria in Vizagapatam	Subbarao and Apparao
	Malaria in Salsette Island	Viswanathan
	Malaria in Pandharpur	Soman

INDIAN JOURNAL OF MALARIOLOGY.

Vol II, Nos 1 and 2 (March/June 1948)	Chloroquine (SN 7618) in Malaria	Chaudhuri *et al*
	Malaria Transmission	Senior White
	Prophylactic Use of Paludrine in a Tea Estate	Ray
	The Distribution of Anopheline Mosquitoes in India Part V	Puri
Vol II, No 3 (September 1948)	Spraying Equipment in Malaria Control with D D T	Ramakrishnan and Rama Krishna
	Clinical Trials of Cam Aqui in Malaria	Chaudhuri and Chakravarty
	Measurements of Malaria Part II	Dakshinamurty
	[illegible]	Viswanathan and Rao
	[illegible]	Jaswant Singh
	[illegible]	Godbole *et al*
	[illegible]	Indian Research Fund Association
Vol II, No 4 (December 1948)	[illegible]	Sen
	[illegible]	Sen
	[illegible]	Ramakrishnan *et al*
	[illegible]	Bhatia
	[illegible]	Rao
	Antimosquito Operations in Cuttack Town	Hajra
	Malaria in Khandwa Tahsil	Subrahmanian and Dixit
	Letter regarding ' Dosage of Paludrine	Mungavin
Vol III, No 1 (March 1949)	[illegible]	Adhikari and Ganguli
	[illegible]	Raghavan and Krishnan
	[illegible]	Viswanathan *et al*
	[illegible]	Viswanathan
	Sporozoites of Plasmodium in *Anopheles turkhudi* Liston	Bhatt
	Insecticidal Properties of Hexachlorocyclohexanes, D D T and Related Compounds	Kulkarni
	D D T Barrier Spray in *A letifer* Areas	Nair
Vol III, Nos 2 and 3 (June/September 1949)	Control of Rural Malaria with D D T	Jaswant Singh and Dalip Singh
	Transmission Experiments with *P knowlesi*	Jaswant Singh *et al*
	Malaria in Orissa	Venkat Rao
	Trials with D D T as a Larvicide	Nagendra and Narayana Murthy
	Malaria Control in Coorg	Jaswant Singh and Kariapa
	A New Method of Diagnosis of Kala azar	Raghavan
	Napier and Chopra Tests in Kala azar	Raghavan and Satya Prakash
	[illegible]	Mulligan *et al*
	[illegible]	Dakshinamurthy and Sharma
	[illegible] *fatigans*	Raghavan and Misra
	Mf malayi Brug in *C fatigans* and *A stephensi*	Raghavan and Krishnan
	Comments on Man made Malaria in India	Henderson
	Malaria in Tirumalai Village Chittor District	Subramaniam and Chetty
	Letter regarding Dosage of Paludrine	Mungavin

Vol III, No 4 (December 1949)		Sen
		Viswanathan and Rao
		Venkat Rao
		Jaswant Singh *et al*
		Vedamanikkam
		Subramanian *et al*
		Jaswant Singh and David
		Jaswant Singh
		Chaudhuri and Rai Chaudhuri
		Chaudhuri and Rai Chaudhuri
		Banerjea
		Jaswant Singh *et al*
		Jaswant Singh *et al*
		Jaswant Singh
Vol IV, No 1 (March 1950)	Malaria and its Vectors in Borneo	McArthur
	Malaria Transmission in Udaipur State	Subramanian and Sen Gupta
	Suppressive Action of Antimalarial Drugs	Jaswant Singh *et al*
Vol IV, No 2 (June 1950)		Chaudhuri and Chakravarty
		Chaudhuri and Poti
		Chaudhuri *et al*
		Srivastava
		Mohan
		Ghosh
		Jaswant Singh
		Jaswant Singh *et al*
		Jaswant Singh and Nair
		Jaswant Singh *et al*
		Hamilton
		Bami
		Venkat Rao and Ramakrishna
		Jaswant Singh
Vol IV, No 3 (September 1950)		Tyssul Jones
		Jacob
		Senior White and Adhikari
		Kruse and Konchady
	ɔsa	Chano *et al*
		Chow *et al*
		Watson *et al*
		Jaswant Singh *et al*
		Jaswant Singh *et al*
		Jaswant Singh and Raghavan
		Jaswant Singh
		Ramakrishnan and Satya Prakash
	Studies on *Plasmodium berghei* Part II	Ramakrishnan and Satya Prakash
		Colless
		Kar
		Jaswant Singh

...o 4 (...ber 1950)		McArthur
		Venkatraman
		Jaswant Singh *et al*
		Jaswant Singh and Nair
	Malaria in Southern Formosa	Watson and Liang
	Efficacy of D D T in Malaria Control	Viswanathan and Gadre
	Use of Benzene Hexachloride as Residual Insecticide	Viswanathan *et al*
	Anopheles Densities in Indoor Shelters	Viswanathan *et al*
...ol V, No 1 (March 1951)		Rajendram and Jayewickreme
		Rajendram and Jayewickreme
		Tyssul Jones
		Tyssul Jones
...ol V, No 2 (June 1951)		Venkat Rao
		Najib Khan *et al*
		Gilroy
		Colless
		Chow *et al*
		Rajindar Pal
		Raghavan
		Dakshinamurty and Sharma
		Dakshinamurty and Sharma
		Jaswant Singh *et al*
	Mosquitoes	Jaswant Singh *et al*
		Jaswant Singh *et al*
		Viswanathan
		Viswanathan
		Dhaliwal
	...alaria	Jaswant Singh
Vol V, No 3 (September 1951)	Bionomics of *A aquasalis* Part I	Senior White
	Clinical Trial of M 5943	Chaudhuri *et al*
	Action of Proguanil and Pamaquin against *P knowlesi*	Ray *et al*
	Toxicity of Proguanil in *S rhesus* Monkeys	Nair *et al*
	Isolation of *P* ...*inui* from Mixed Infection	Jaswant Singh *et al*
	Studies on *Plasmodium berghei* Part III	Ramakrishnan *et al*
	Studies on *Plasmodium berghei* Part IV	Ramakrishnan *et al*
...ol V, No 4 (December 1951)	Bionomics of *A aquasalis* Part II	Senior White
	Nocturnal activities of *A fluviatilis*	Jaswant Singh and Mohan
	Fungus resembling plasmodial sporozoites in *A annularis*	Jaswant Singh *et al*
		Jaswant Singh *et al*
		Jaswant Singh *et al*
		Jaswant Singh *et al*
		Rajindar Pal *et al*
		Chow *et al*
		Srivastava and Diwan Chand Srivastava
		Jaswant Singh

Vol VI, No 1 (March 1952)	Courses in Malariology	Jaswant Singh
	Bionomics of *A aquasalis* Part III	Senior White
	Irrigation and mosquitoes in U S A	Henderson
	Nocturnal behaviour of *A minimus*	Krishnaswami
	Prophylactic trials against *P gallinaceum*	Jaswant Singh *et al*
Vol VI, No 2 (June 1952)	Effect of proguanil suppression on B N Railway	Adhikari and Ganguli
	Residual Insecticidal Studies	Bhatia
	Screening of Antimalarials against *P gallinaceum* Part I	Jaswant Singh *et al*
	[illegible]	Ray *et al*
		Jaswant Singh *et al*
		Satya Prakash *et al*
		Jaswant Singh *et al*
		Ramakrishnan
		Viswanathan *et al*
	Rural Malaria Control with Residual Insecticides	Subramanian and Vaid
Vol VI, No 3 (September 1952)	Organic Synthetic Insecticides in Malaria Control	Jaswant Singh and Rajindar Pal
	[illegible]	Rajindar Pal *et al*
		Rajindar Pal
		Rajindar Pal and Sharma
		Viswanathan
		Rajindar Pal and Sharma
		Rajindar Pal and Sharma
		Rajindar Pal *et al*
		Sharma and Rajindar Pal
		Rajindar Pal
		Rajindar Pal *et al*
	Sprayers	Rajindar Pal
Vol VI, No 4 (December 1952)	Economic Status of Villagers before and after D D T Spraying	Bhombore *et al*
	Seasonal Variation in Breeding Places of *A fluviatilis*	Vedamanikkam
	Malaria Control Measures in the Terai Area	Srivastava and Chakrabarti
	D D T as a Mosquito Larvicide	Tyssul-Jones
	Blood of Normal and Malarial Chick Infected with *P gallinaceum*	Rama Rao and Giri
	Distribution of Human Plasmodia in India	Jaswant Singh *et al*
	[illegible] Malaria Part I	Jaswant Singh *et al*
		Jaswant Singh *et al*
		Jaswant Singh and Ray
		Jaswant Singh *et al*
		Ramakrishnan *et al*
		Jaswant Singh *et al*
		Rao *et al*
		Brooke Worth and Sitaraman
Vol VII, No 1 (March 1953)	Malaria in the Maldive Islands	Iyengar *et al*
	Pyrimethamine in Human Malaria	Srivastava *et al*
	Pyrimethamine in Human Malaria	Jaswant Singh *et al*
	4 aminoquinolines in Single Dose Treatment of Malaria	Jaswant Singh *et al*
	[illegible]	Jaswant Singh *et al*
		Jaswant Singh *et al*
		Siddon
		Ramakrishnan
		Ramakrishnan *et al*
		Ramakrishnan *et al*
		Gramiccia and Sacca

[V]I No 2 [(June 19]53)	Studies on *P berghei* Part XI	RAMAKRISHNAN *et al*
	Studies on *P berghei* Part XII	KRISHNASWAMI *et al*
	Host Predilection of *A fluviatilis*	RAMAKRISHNAN AND SATYA PRAKASH
	Experimental Infections in Domestic Pigeons	DAVID AND KRISHNAN
	Screening of Antimalarials against *P gallinaceum* Part II	JASWANT SINGH *et al*
	Avian Plasmodium in Indian Birds Part I	RAY AND BHATNAGAR
	Anopheline Fauna of a Hill Tract in Mysore State	BROOKE WORTH
	Recent Advances in Synthetic Antimalarials	BAMI
	Gonotrophic Discordance in *A annularis*	VENKAT RAO AND ANNAJI RAO
[V]ol VII, No 3 (September 1953)	Studies on *P berghei* Part XIII	RAMAKRISHNAN *et al*
	Studies on *P berghei* Part XIV	KRISHNASWAMI *et al*
	Toxic Manifestations of Repeated Doses of Pyrimethamine	JASWANT SINGH *et al*
	4 aminoquinolines against *P cynomolgi*	JASWANT SINGH *et al*
	Avian Plasmodium in Indian Birds Part II	RAY *et al*
	Nuri Strain of *P knowlesi* Part I	JASWANT SINGH *et al*
	Effect of Milk Diet on *P gallinaceum*	RAMAKRISHNAN *et al*
	J S B Stain—Its Preparation in Powder Form	JASWANT SINGH *et al*
	Liver Injury Associated with Malaria	RAY
	Malaria Control for Rural and Urban Areas	RAO *et al*
	Metabolic Studies with Bromoguanide	BAMI
	Studies on 8 aminoquinolines	JASWANT SINGH *et al*
[Vol] VII No 4 [(De]cember 1953)	Symposium on pyrimethamine Opening address	JASWANT SINGH
	Pyrimethamine and its estimation	BAMI
	Effect of vitamin B 2 on the toxicity of pyrimethamine	RAMALINGASWAMI AND SRIRAMACHARI
	Trials with pyrimethamine	RAY
	Antirelapse properties of pyrimethamine	RAY *et al*
	Screening of antimalarials against *P gallinaceum* Part III	
	Synergistic action of quinine and pyrimethamine	RAY *et al*
	Pyrimethamine in the sporogony cycle of *P gallinaceum*	JASWANT SINGH *et al*
	Pyrimethamine in malaria	JASWANT SINGH *et al*
	Field trials with pyrimethamine	CHAUDHURI
	Clinical trial of pyrimethamine and amodiaquin	KOLEKAR
	Drug fever leucocyte counts erythrocyte sedimentation rate and urine after pyrimethamine	KHATRI AND SAM[...]
	Acute malaria treated with pyrimethamine	LAHA *et al*
	Trials with pyrimethamine resochin amodiaquin and quinine	LAHA *et al*
	Susceptibility of *P cynomolgi* infection to pyrimethamine proguanil and bromoguanide	SRIVASTAVA
	Resistance to pyrimethamine in *P cynomolgi*	NAIR *et al*
	Nuri strain of *P knowlesi* Part II	JASWANT SINGH *et al*
	Symposium on pyrimethamine Critical review	NAIR *et al*
Vol VIII No 1 (March 1954)	Screening of antimalarials against *P gallinaceum*	JASWANT SIN[GH]
	Studies on *P berghei* Part XV	JASWANT SINGH
	Egg of *Anopheles gigas gigas*	KRISHNASWAMI
	Relationship between the physical state of chlorinated insecticides to their biological effectiveness	NARAYANDAS
	Relationship between the lipoid solubility of D D T and its contact toxicity	RAJINDAR P
	Control of *C fatigans* by D D T larvicide	RAJINDAR P
	A first record of *A theobaldi* from Mysore State	PARTHASAR[ATHY]
	Anophelines in western hill tracts of Mysore State	BHOMBORE
	Effect of lime on residual activity of D D T	BHOMBORE
	Treatment of malaria with a single dose of amodiaquin	BHOMBORE
		PATEL AND D[...]AL

Vol VIII, No 2 (June 1954)		Fli Chernin
		Ramakrishnan
		Ramakrishnan
		Ramakrishnan
		Ramakrishnan
		Satya Prakash
		Jaswant Singh *et al*
		Jaswant Singh *et al*
		Narayandas and Ray Gupta
	Judging the effectiveness of residual toxicity of insecticide deposits	Bhombore *et al*
Vol VIII, No 3 (September 1954)	Studies on Nuri strain of *P knowlesi* Part III	Jaswant Singh *et al*
	Studies on Nuri strain of *P knowlesi* Part IV	Jaswant Singh *et al*
	Studies on Nuri strain of *P knowlesi* Part V	Jaswant Singh *et al*
	Fresh approach on relapse mechanism in malaria	Jaswant Singh and Ramakrish
	Liver enlargement during acute infection in simian malaria	Ray and Nair
	Antimalarial action of the active metabolite of bromoguanide	Ray *et al*
	Malaria problem in Bhuj	Satya Prakash
	Method of testing the toxicity of residual insecticides	Afridi *et al*
Vol VIII, No 4 (December 1954)	Symposium on *P berghei* Introduction	Jaswant Singh
	History of discovery of *P berghei*	Berghe
	Natural history of *P berghei*	Vincke
	Experimental transmission of *P berghei*	Vincke
	Mosquito transmission of *P berghei*	Bray
		Schneider
		Maegraith
		Raffaele
		Jaswant Singh *et al*
		Ray and Bose
		Greenberg and Coatney
		Ramakrishnan
		Sergent
	Immunology of *P berghei*	Fabiani
	Immunity to *P berghei* infection in mice	Galliard and Lapierre
	Absence of cross immunity between *P berghei* and *P vinckei*	Rodhain
	Immunity to *P berghei*	de Smet and Frankie
	Host parasite relationships between albino rat and *P berghei*	Corradetti *et al*
Vol IX, No 1 (March 1955)	Filariasis in Mangalore (South India)	Krishnaswami
	Day time resting habits of *A culicifacies*	Ariaratnam
	Chemical and photodynamic deterioration of D D T	Srivastava *et al*
	Comparative effectiveness of D D T, B H C, and Dieldrin	Rajindar Pal *et al*
	Efficacy of D D T, B H C and Dieldrin	Viswanathan *et al*
Vol IX, No 2 (June 1955)	Susceptibility of *C bitaeniorhynchus* to *P relictum*	Jaswant Singh and Mohan
	Susceptibility of *Ædes* mosquitoes to *P gallinaceum*	Mohan
	Infection in *A fluviatilis* and *A stephensi* with *P falciparum*	Mohan
		Mohan
		David and Nair
		Menon and Nair
		Nair *et al*
		Misra and Dhar
		Subramaniam
		Pritam Singh
		Inder Singh

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TABLE OF CONTENTS

VOL IX

No 1 (MARCH 1955).

Page

No 2 (JUNE 1955).

IX, No 3	Biochemistry and nutrition of *P berghei*	FULTON AND SPOONER
ember 1955)	Studies on *P berghei* Part XXI	CHAKRABARTI
	Types of tuberculosis in rhesus monkeys	NAIR AND RAY
	Studies on Nuri strain of *P knowlesi* Part VIII	NAIR AND RAY
	Studies on Nuri strain of *P knowlesi* Part IX	RAY AND NAIR
	[illegible]	SRINIVASAN AND RAJAH
	[illegible]	PETERS *et al*
	[illegible] with	
	[illegible]	BHOMBORE *et al*